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OF
DERMATOLOGY AND SYPHILOLOGY

(*Succeeding Vol. 38, 1919, the Journal of Cutaneous Diseases*)

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Archives of Dermatology and Syphilology

Volume 2 JULY, 1920 Number 1

LICHEN NITIDUS

RICHARD L. SUTTON, M.D.
KANSAS CITY, MO.

LITERATURE ON LICHEN NITIDUS

Lichen nitidus was first described by Pinkus,[1] in 1901, and in an exhaustive paper on the subject, which he contributed to Neisser's Festschrift, in 1907, the Berlin dermatologist gave a detailed clinical and histologic report of nine cases of the disorder. Since that time, examples have been recorded by Arndt[2] Kyrle and McDonagh,[3] Reines[4] and Bachrach,[5] in England and on the Continent, and by myself[6] in this country. It is probable, as Pinkus has suggested, that the disorder is not nearly so rare as the literature would indicate. Owing to the absence of subjective symptoms, many cases are undoubtedly overlooked.

The disease is characterized by the presence of one or more irregular patches, or collections, of numerous smooth, slightly elevated, rounded, pin-point to pinhead sized, pinkish, flesh-colored papules, some of which are marked by slight central depressions. The mucous membranes are never involved. The presence of the little papules gives rise to no subjective symptoms, and in many instances the discovery of the eruption is accidental. Nearly all of the cases described by Pinkus occurred in males, and in nearly every instance the penis and the lower part of the abdomen were involved. In a few instances, the forearms also were affected.

---

1. Pinkus: Behand. d. Berlin. Dermat. Gesell. **12:** No. 3, 1901. Ueber eine neue knötchenförmige Hauteruption: Lichen nitidus, Arch. f. Dermat. u. Syph. **85:**11, 1907.

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3. Kyrle, J., and McDonagh, J. E. R.: Beitrag zur Kenntnis des Lichen Nitidus, Arch. f. Dermat. u. Syph. **95:**45, 1909; Brit. J. Dermat., 1909, p. 339.

4. Reines, S.: Zur Kenntnis eines eigentümlichen Knotchenausschlags (Lichen nitidus Pincus), Med. Klin. **6:**1180, 1910.

6. Sutton, R. L.: Lichen Nitidus, J. Cutan. Dis. **28:**597, 1910.

5. Bachrach: Kasuistischer Beitrag zur Kenntnis des Lichen nitidus, Dermat. Ztschr. **20:**189, 1913.

6. Sutton, R. L.: Lichen nitidus, J. Cutan. Dis. **28:**597, 1910.

Kyrle and McDonagh's patient was a young woman, and the distribution of the eruption was more or less general, the parts principally affected being "the flexor surfaces of the joints, especially wrists and elbows, the axillae and anterior axillary folds, inguinal regions and genitocrural folds, popliteal fossae, and both malleolar regions." In the case reported by Reines, the eruption was confined mostly to the penis and scrotum, and in the one described by Bachrach, to the trunk, the left thigh, and the left hip joint. In my first case, the upper part of the chest, near the anterior axillary folds, the lower abdomen and the forearms were the sites of attack.

PATHOLOGY OF THE DISEASE

The cause of the disease is not known. Kyrle and McDonagh believe it to be tuberculous. Bachrach's patient was tuberculous, but the lichen nitidus lesions did not react to tuberculin. In the cases described by Reines and by me there was no reaction to tuberculin, and attempted animal inoculations met with no success. Arndt has made a careful and exhaustive study of the histopathology, his conclusions being based on the examination of serial sections from 148 lesions. He found a sharply limited, subepithelial infiltration in the most superficial layers of the cutis, the mass structurally resembling that of a tubercle. The epithelial alterations varied somewhat in the different cases, and even in different nodules from the same case. He found the most striking feature of the histology to be the frequent occurrence of giant cells; this naturally suggested a tuberculous etiology, but careful investigation along other lines did not support this view. Tubercle bacilli were absent, and both animal inoculations and tuberculin tests gave negative results. In addition to the giant cells, Arndt found numerous epithelioid cells and mononuclear round cells in the infiltrate. Many of the epithelioid cells were pigmented. The tubercle-like structure was most marked in the older lesions, but in these, unlike true tubercles, there was a fair number of blood vessels. In the recent nodules, there was merely a round-cell infiltration. The epithelium overlying a nodule was sometimes thinned, and more or less parakeratotic. Occasionally, there was a gap between the overlying epithelial bridge and the surface of the dermal infiltration.

DIFFERENTIAL DIAGNOSIS

Clinically, the disorder is to be differentiated from lichen planus, multiple verrucae, folliculitis of the penile skin, lichen scrofulosus, and the lichenoid syphiloderm. Of these affections lichen planus is the closest imitator, and in some instances a histologic examination may be required before a definite conclusion can be reached. In the process of differentiation, Arndt says that the most vital points are

PLATE 1

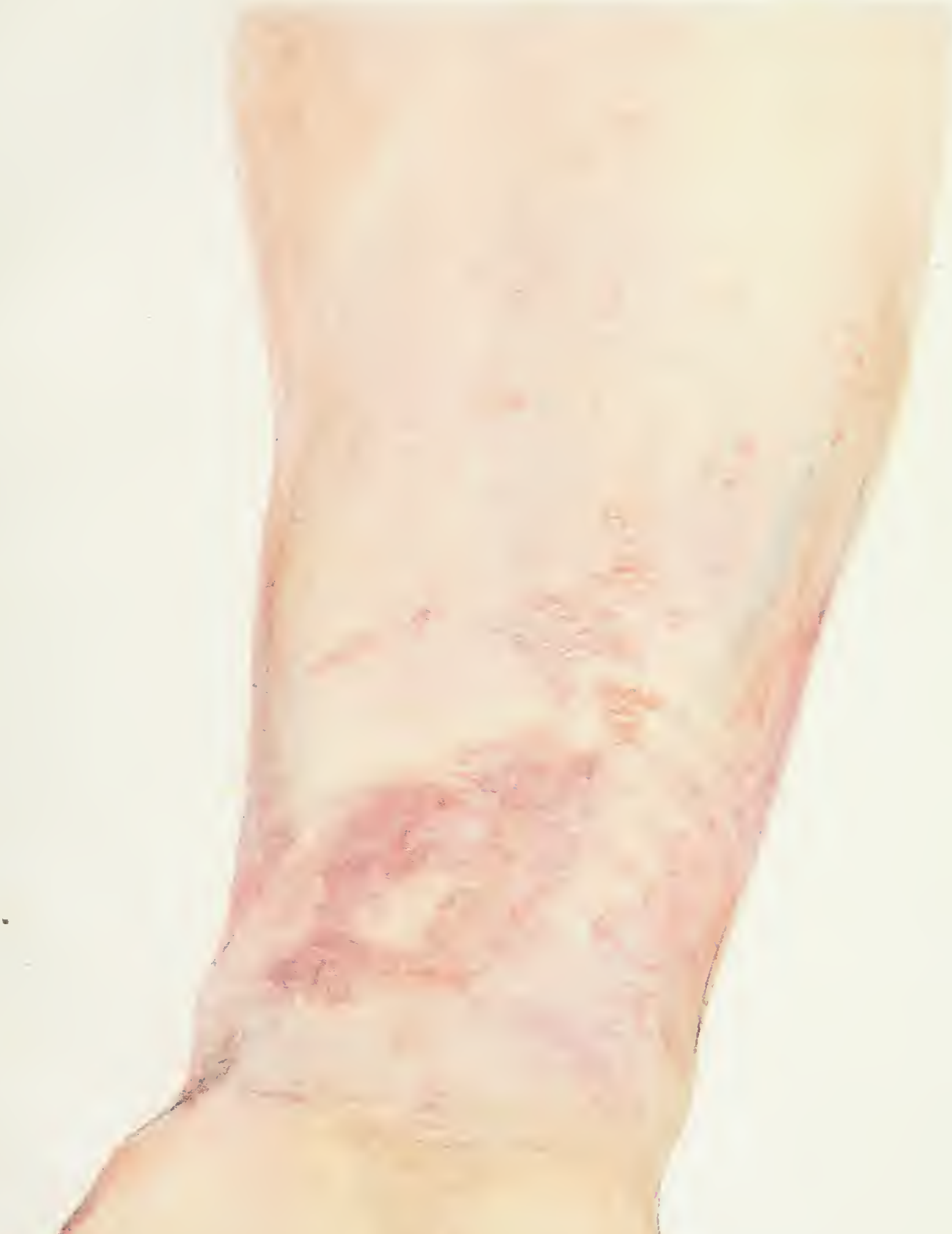

Plate 1.—Lichen nitidus, showing character and distribution of lesions (Slightly enlarged.)

the color, the uniformity of the lesions, the absence of grouping, and the freedom from subjective symptoms.

Recently I had an opportunity to study a well developed case of lichen nitidus in which the color, lack of uniformity and distribution of the lesions all were suggestive of lichen planus.

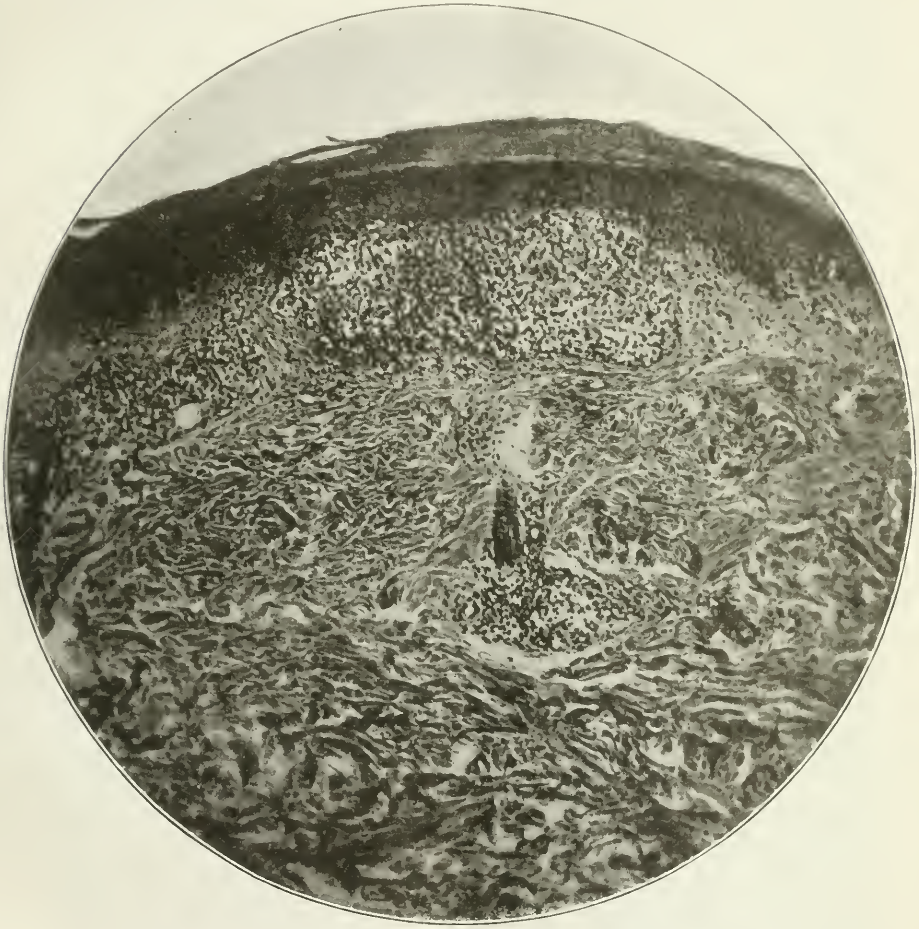

Fig. 1.—Lichen nitidus, showing typical cellular infiltration; low magnification. (Photomicrograph by Dr. George M. MacKee.)

REPORT OF CASE

History.—The patient was a farmer, aged 27, referred to me by Dr. John C. Ottman of Craig, Mo. The family history was negative for tuberculosis. The case was of eighteen months' duration, and the lesions, which involved the forearms, the backs of the hands, the abdomen, and the anterior surfaces of the thighs, had first been discovered on the dorsal surfaces of the hands. At no time had their presence given rise to subjective symptoms of any kind.

Examination.—On examination, the patient was found to be a well-developed, muscular, rugged young man, with light brown hair and eyes. He was 5 feet and 11 inches tall, and weighed 164 pounds. There was no history of his ever having had a more serious illness than varicella, and a complete physical examination, made by my assistant, Dr. Sherman Mella, showed him to be above the normal in development and condition. The Wassermann test was negative, and there was absolutely no reaction to tuberculin (subcutaneous injection). The most characteristic lesions were to be found irregularly scattered over the flexor surfaces of the forearms. In these localities the slightly elevated, pinkish or reddish, flesh-colored, oval or flat-topped papules were interspersed with areas of normal skin, and exhibited but little tendency to grouping or coalescence. A few were marked by minute, central depressions. At the wrists the little lesions were more closely placed, six or eight, or even more, sometimes occupying a space no larger than the top of a lead pencil. Here the color, also, changed. Instead of being pinkish or yellowish in hue, the papules were reddish or violaceous, and on the lateral and dorsal surfaces of the wrists this variation in color was even more striking. On the backs of the hands, grouping, and even apparent coalescence, had occurred, and in some places the affected skin was almost purple in color. The surface of the lesions, however, was invariably smooth and the skin comparatively soft, the hyperkeratinization so characteristic of long-standing patches of lichen planus being entirely absent. Subjective symptoms likewise were wanting. Over the abdomen and thighs, the lesions were more sparsely distributed, and in these localities they bore a considerable resemblance to those of lichen scrofulosus.

Microscopic Study.—For histologic study, six small pieces of tissue were excised at various points on the forearms and hands. These were fixed, hardened, sectioned and stained for me by Dr. Watson Campbell. The solitary tumors differed but little from those seen in my first case, and those so admirably described by Arndt, and by Kyrle and McDonagh. In the older and apparently more characteristic lesions, pigmentation of the epithelioid cells was somewhat more marked, and giant cells more frequent than in the earlier papules. In sections from one of the earlier lesions, the vascular changes were such as to lead one to suspect that a small capillary was the anatomic structure primarily involved. The minute, ball-shaped mass of small round cells completely surrounded the tiny arteriole, and impressed the observer with the idea that the destruction of the canal, by occlusion of the caliber, would have been a matter of only a short time. In the closely grouped, violaceous lesions on the backs of the hands, no instance of actual coalescence was discovered, although in some of the specimens the little subepidermal growths were so closely placed that three, and in one instance four, occurred in a single low power field. There was no evidence of caseation, and apparently the lesions were in no way connected with the follicles or coil glands.

COMMENT

Owing to the complete failure to react to tuberculin, animal inoculations were not attempted.

The case is of interest because of the comparative rarity of the disorder, the character and distribution of the eruption, and the patient's freedom from demonstrable tuberculous lesions of any kind.

A MELANOTIC TUMOR OF THE LIP TREATED WITH RADIUM

DOUGLASS W. MONTGOMERY, M.D.

AND

GEORGE D. CULVER, M.D.

SAN FRANCISCO

It has been strongly advised, and by one whom we all rightfully regard as an authority on the use of radium in malignant growths, not to employ either radium or roentgen rays in melanotic tumors.[1] Like all general rules, however, it is subject to exceptions, probably even in the mind of this authority. The following case shows a fortunate outcome in transgressing the rule.

REPORT OF A CASE

History.—Nov. 6, 1918, a physician, aged 37, consulted us in regard to a dark, slate blue, circular spot about 3 mm. in diameter, lying deep in the exposed red part of the lower lip. It was near the cutaneous border in the median line, and had been first noticed perhaps four years before. He thought it had doubled in size in the past two years. It did not clear up on pressure, but became more distinct, and there was a dusky shadow extending out beyond the central dark spot. The lesion was not palpably demonstrable. There were no subjective symptoms, and there was no adenopathy. The entire lip was slightly scaly, and the skin was seborrheic.

The patient's father was subject to moles, and died of an operation following Banti's disease; the mother was still living, enjoyed good health, and was only sixteen years older than her son.

Pigmented spots on the lips must not be regarded for this reason alone as being malignant, but the dark slate color of this one, its steady growth, and its apparent extension by infiltration, as shown by the dusky shadow beyond it, caused us to suspect sarcoma.

Treatment and Course.—A strong radium plaque, the size of a ten-cent piece, and containing 24.23 mgm. of radium element, was screened with 0.40 mm. of lead, four thicknesses of writing paper, and one thickness of rubber tissue, and was retained in place for one hour.

A definite decrease in size was noticed in thirty-six hours, and the color changed from a deep slate blue to gray. A radium reaction set in nine days after the application, when the surface became red, scaly and felt sunburnt. At the same time, there was noticed a tender area with some swelling of a lymph node under the right side of the jaw.

On December 2, the dark spot had decreased to a dot 1 mm. in diameter. Two days before this, a slate colored spot 2 by 1.50 mm. was noticed just within and below the left corner of the mouth. The affection now looked more than ever like a malignant growth.

The same radium plaque with the same screening was applied to the newly discovered lesion for one hour.

---

[1] Wood, Francis C.: Cancer, Nelson Loose-Leaf Medicine, 1919, p. 35.

By December 18, the lesion on the lip was reduced to a dull surface. The reaction over the lesion in the left cheek had begun about a week after the application of the radium, and by this time—in a little over two weeks—the lesion was less prominent and was covered by a gray haze, through which the blue color, which also seemed to be decreasing, could be seen. Another radiation similar to the previous one, but through sixteen thicknesses of paper, was now given. At the same time, two tubes, 25 mgm. each, and screened by one silver tube and 1 mm. of lead, were placed under the left side of the jaw for four hours.

A number of weeks after this radiation, the lesion in the left cheek, which had been receding, began suddenly to enlarge until, on July 1, it was about one-quarter again as large as it had been. Later in July it began to recede. On August 3, another radiation was given to this spot with the same strong plaque, screened by 0.4 mm. of lead and four thicknesses of writing paper. By August 12, the patient said the lesion had disappeared, and when we saw it August 26, there was a faint blue streak in this situation as from a vein glimmering through the mucous membrane; there were two dimples in the surface as from the absorption of tissue. There was, however, no evidence of a tumor either there or in the lip, nor has there been any evidence of recurrence since.

In this case, the alternatives would have been either to allow the affection to pursue its own course, or to perform an extensive and deforming operation. After due consideration, it was determined to employ radium, and fortunately, the case turned out well.

CAUSES OF FAILURE OF RADIUM TREATMENT

The unfavorable reports concerning the use of radium in these growths may arise from two causes. One is the well-known, natural tendency of these tumors to rapid dissemination, which was known long before radium was discovered. In spite of this, any rapid dissemination of the tumors after the application of radium tends to be attributed to radium, which is manifestly unfair.

Another reason for the failure of this treatment may be supplied by the pigment. Cellular pigment is, as is well known, a means of defense against the injurious effects of light, and this is the reason why the skin pigments or tans, on being exposed to light; the pigment increases to protect the cell. The gamma rays of radium are electromagnetic, and are of the same nature, but in much finer wavelets than those of light. The presence of cellular pigment may shield the cell nucleus of the neoplasm from injury by these gamma wavelets, and so diminish their effect as to render them useless in destroying these cells, or may even permit them to act so slightly as to be only a stimulant. The reasonable procedure to combat this would be to so screen the radium employed as to get only the very fine gamma wavelets, which are the most highly penetrative, so that they may step across the pigment line of defense, and attack the cell nucleus just as the neoplastic cell divides, when the nucleus is devoid of a nuclear membrane, and therefore least capable of defense.

FRAMBESIA TROPICA (YAWS)

A STUDY OF THE LITERATURE WITH PERSONAL OBSERVATIONS, A CRITIQUE OF ITS SUPPOSED IDENTITY WITH SYPHILIS, AND A BIBLIOGRAPHY

HERMAN GOODMAN, B.S., M.D.
NEW YORK

DEFINITION

Frambesia tropica is a contagious disease, endemic in the tropics and subtropics, caused by the *Spirochaeta pertenuis* (Castellani) and characterized by both early and late eruptive symptoms somewhat suggestive of syphilis.

Synonyms. — The name frambesia tropica was first applied by Sauvages, 1759, from the raspberry-like appearance of the granuloma. Yaws is a common name, especially in English colonies. Pian is the name given by the French. Bouba or boubas is used in the Spanish colonies. The disease has many local names among different aboriginal peoples. Polypapilloma tropicum was the name given by Charlouis; and the name spirochetose cutanée has been given to differentiate the disease from spirochetose généralisée (syphilis).

HISTORY

The claim has been made that frambesia tropica was known to the ancients. It has also been affirmed that it occupied its place under the generic term "leprosy" of the Bible. Like syphilis, frambesia was "discovered" after the discovery of America by Columbus, and Oviedo described the disease as "boubas" in the West Indies, by which name it is still known there. It is interesting to note that one of the earliest works accredited as proving that syphilis in Europe originated in America is entitled "Tratado llamado Fruto de todos los Santos contra el mal de le ysla Espanola hecho por maestre Rodrigo de Isla ciujano vezino de lisboa para comun e general provecho de los pacientes Enfermos de las semejante Enfermedad que vulgarmente es llamado 'Bubas,'" i. e., "Treatise, Entitled, Fruit of All Saints Against the Disease of the Island Espanola by Master Rodrigo de Isla, Surgeon and Citizen of Lisbon, to the Common and General good of Those Suffering from the Disease in Question, Commonly Called 'Bubas.'"

The theory has been advanced that frambesia tropica had its beginning in Africa, and records of outbreaks on slave ships are available. The West Indian planters were in the habit of quarantining all fresh arrivals, and most slaves acquired the disease before being allowed to enter the plantation of their owners.

OCCURRENCE

The disease is endemic in the tropics. Recent reports from some sections of Africa give the incidence of the disease as 50 per cent. In Ceylon, the observation has been made that the disease, common enough in the low lands, is rare or even nonexistent in towns 800 feet above sea level. Other sections of the East Indies report cases; Australia, Northern Africa and South America have cases of the disease. Our recently acquired possessions, the Philippines, Guam and Porto Rico, report cases. I saw instances of the disease in Porto Rico and in Panama. Cases have been reported in the United States in travelers, and in returned soldiers and sailors, and several doubtful endogenous cases have been reported in the South. During my service at the New York Skin and Cancer Hospital, but one case resembling yaws was seen among over 15,000 patients. This case was that of a Philippine mess boy, and in the light of experience since acquired, I doubt that this was a case of frambesia.

Age.—No age is spared, but it usually occurs prior to puberty.

Sex.—Frambesia tropica occurs equally in both sexes.

Color.—The black and colored races are more prone to the disease. There are fewer whites in the tropics, and ordinarily they live under a better regimen. Two of my cases occurred in white people, two in negroes and the rest in high mulattoes.

ETIOLOGY

Many organisms had been advanced as the cause of frambesia, but it is generally agreed that the *Spirochaeta pertenuis,* discovered by Castellani in February, 1905, on the island of Ceylon, is the etiologic factor. It is interesting to note that this discovery slightly antedated Schaudinn's demonstration of the *Spirochaeta pallida,* March, 1905 (published May, 1905), and that in another section of the globe — West Africa—Wellmann independently demonstrated a spirochete in frambesia in July, 1905.

Spirochaeta pertenuis, like the organism of syphilis, stains with difficulty, and for a time Castellani named his organism *Spirochaeta pallidula.* The spirochete is extremely delicate, motile, spiral shaped, from a few microns to 18 or 20 in length, and an organism about the size of a red blood corpuscle has eight turns. Some examples of the *Spirochaeta pertenuis* are thicker than others, but Castellani did not think that too great importance should be given to slight morphologic details. The spirochete of yaws is indistinguishable from the corresponding germ of syphilis; and Schaudinn, to whom Castellani sent samples of this organism, so declared himself. Russell has pointed out six characters that are different.

Spirochaeta pertenuis is constant in the skin lesions of frambesia tropica. The smear should preferably be made from a fresh lesion, not secondarily contaminated. The crust of the lesion is removed, and a sterile platinum loop passed over the moist raspberry granulation, and then smeared over the slide, fixed and stained by Giemsa's stain. The dark field method, or the India Ink (Burri) method may be utilized.

The organism is demonstrable in the spleen, lymphatic glands and bone marrow. The circulating blood is infectious, but the organism has not been demonstrated. Neither microscopic examination nor animal inoculation has been positive for cerebrospinal fluid.

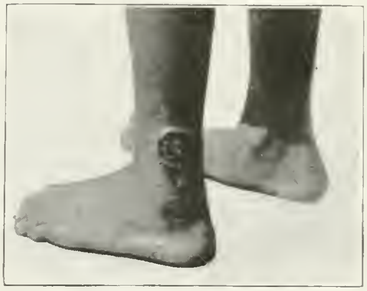

Fig. 1.—Frambesia tropica (yaws); primary or mother yaw—usually extragenital. (From report of commissioner of health, Porto Rico.)

The organism has been cultivated in vitro and in vivo. The sterile tissue technic of Noguchi is utilized.

CONTAGIOUSNESS

A break in the skin surface is believed, as in syphilis, to be essential for the *S. pertenuis* to gain a foothold on the new host. Such a break in continuity is common enough in the poor of the tropics, who seldom are completely covered with clothes, and who are a constant prey for all kinds of biting insects.

It is probable that *S. pertenuis* may be transmitted through an intermediate carrier, such as flies. Experimentally, flies have successfully transmitted the disease, having first been allowed to rest on open yaw lesions. The *S. pertenuis* has also been recovered from such flies.

COURSE OF THE DISEASE

Incubation Time.—The incubation time is given as from ten days to several weeks. It is difficult to get a history, and none of my patients could give me any data on this.

Initial Lesion.—The initial lesion or "mother yaw" occurs at the site of inoculation. It is nearly always extragenital in location, and only occasionally multiple. The initial lesion may begin as a conical papular elevation, which necroses in the center and becomes incrusted with a moist, papillomatous surface under the crust. Pruritus may be present. The primary lesion of frambesia may resemble the later lesions, and some do not consider it the primary lesion, in the sense that the syphilitic chancre is primary, but that the "mother yaw" is the first lesion of the general eruption. The primary lesion often persists well into the generalized stage.

In many cases it is impossible to get a history of any primary lesion. In one of my cases, that of a woman who had been previously examined, and found free of lesions, a generalized secondary frambesia was the first indication of the infection. She gave no history of an initial lesion.

Generalized Stage.—The lesions of the generalized stage appear from one to three months after the first appearance of the primary yaw. There may be a hundred lesions, more or less. The individual lesions are papular, from the size of a pea to that of a nickel or larger. A furfuraceous eruption has been described as preceding the papular yaw lesion, and even as persisting throughout the attack. I have never observed this. The fullfledged lesion is covered by a yellow dry crust, on removal of which one sees the raspberry-like excrescence typical of the disease, moist and rich in spirochetes. The resemblance to the raspberry is marked, especially in fresh lesions. If untreated, the lesions may persist from two to four months, and unless badly contaminated, they will heal spontaneously.

Special names have been given to frambesia tropica, according to the location and the formation of the lesion. Thus, circinate or ringworm yaws has been described; and yaw lesions of the palms and soles modified by the thickness of the epidermis and the continual traumatism have received special appellations. Castellani has described a peculiar pitted lesion of the palms and soles.

The distribution is habitually on the exposed parts, rarely on the scalp, although I saw one case with multiple scalp lesions. Mucous membranes are ordinarily not affected, but the mucocutaneous junction may be the site of lesions. The genitals are occasionally affected, and I saw the development of a secondary yaw on the foreskin, which

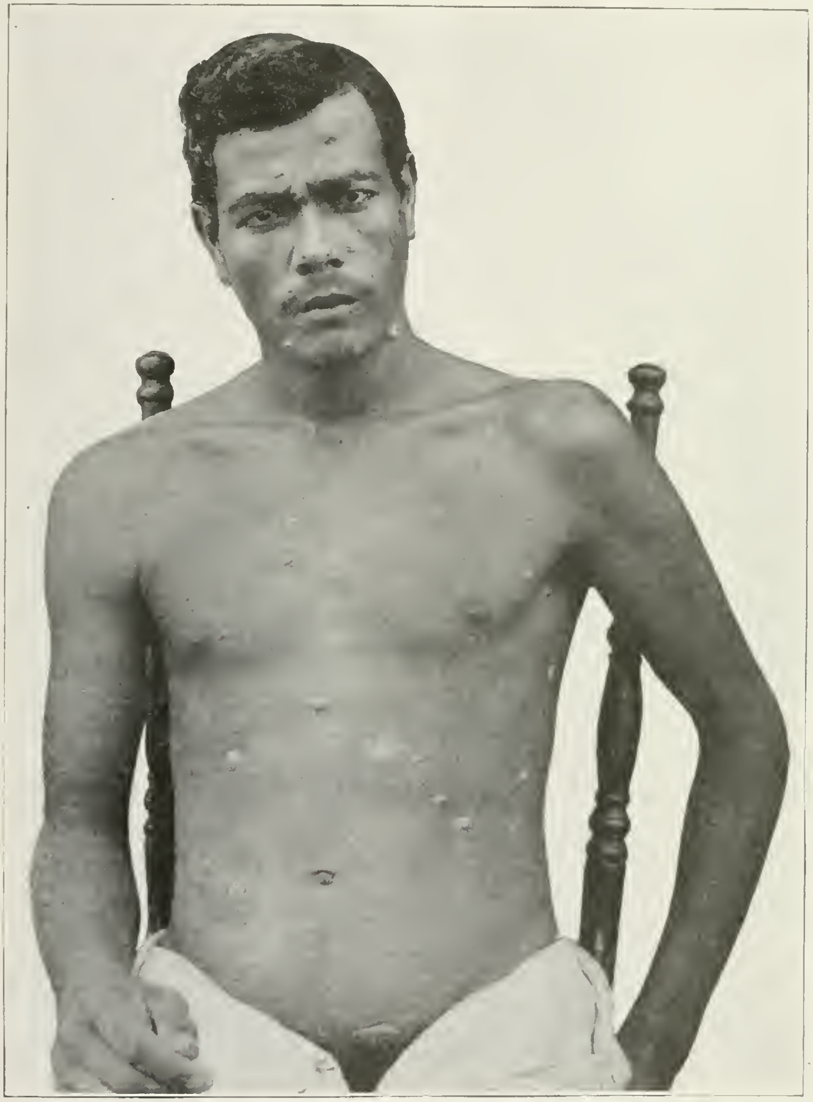

Fig. 2.—Frambesia tropica; primary yaw in pubic hair line; generalized secondary frambesia. (From report of commissioner of health, Porto Rico.)

I was led to believe had been self inoculated. I also saw a sadly neglected case with marked lesions in the axillae and groin. The hair is not affected, and alopecia does not result. The glands are not constantly enlarged. Visceral lesions are rare, but bone and joint lesions were present in 20 per cent. of selected cases, as evidenced by the roentgen ray. The general health is not affected, but many patients have slight fever and rheumatic pains. There may be new crops of lesions, either while former crops are still present or after a period of recession.

The blood picture is unreliable because most patients suffer with a concomitant helminthiasis.

Tertiary Stage.—Tertiary yaws as a distinct phase of frambesia tropica is still questioned. It is said to come within a year of the generalized rash, or to follow without interval; the secondary stage passing directly into the tertiary. One must be extremely cautious not to confuse tertiary yaws with a concomitant tertiary syphilis and the tendency to ulceration of nearly all tropical eruptions should always be considered. Extensive scarring with a history of frambesia tropica should not be taken as evidence of tertiarism. The destructive nasopharyngeal condition known as gangosa has been considered a tertiary yaw lesion. I saw one example in Porto Rico of such an ulceration, but was not able to follow the patient, as he was a temporary prisoner and soon passed to freedom. It would be difficult also to rule out syphilis as the cause of such an ulceration, and on the island of Haiti, I saw numerous extensive nasopharyngeal ulcerations ascribed to syphilis. One author has, unjustly I think, described juxta-articular nodules as tertiary stage frambesia.

NERVE LESIONS

Spirochaeta pertenuis has not been demonstrated in the cerebrospinal fluid either by microscopic examination or by experimental animal inoculation. There is but one reference to the existence of a frambesia-form general paresis, or tabes dorsalis. The observer working among Fijians, who are said to be free from syphilis, admits in his report that the "Fijian is a difficult subject to examine for nervous diseases." Every other observer has commented on the absence of nervous symptoms, and iritis has never been noted.

HEREDITARY TRANSMISSION

Frambesia tropica is not hereditary. Among numerous births in yaws hospitals, no case of an infant born with lesions has been observed. There is a report of frambesia acquired at birth with the

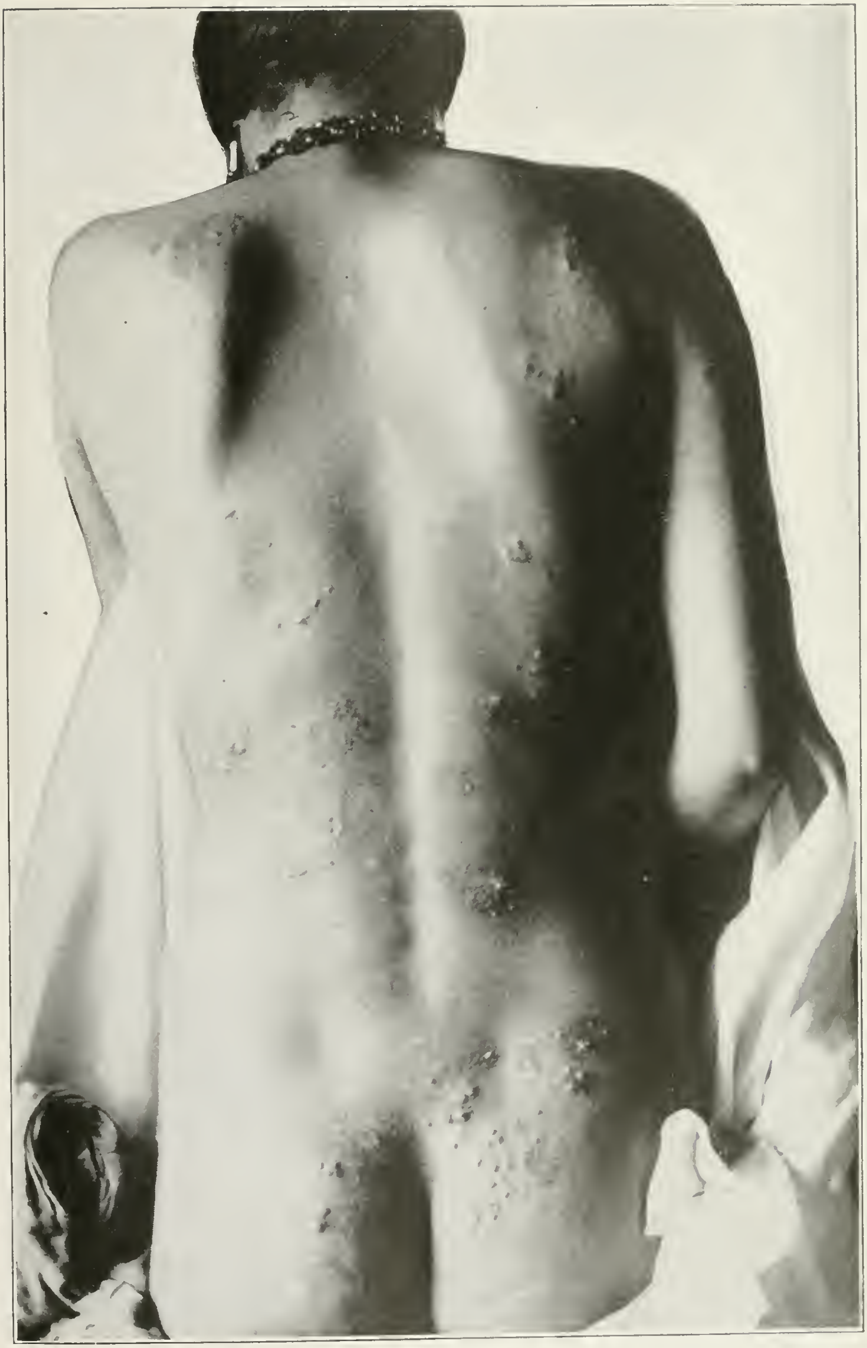

Fig. 3.—Generalized eruption of the second stage of frambesia tropica. (From report of commissioner of health, Porto Rico.)

first lesion appearing at twenty days; and a second report of a child who sustained a scratch on the face immediately after birth in a yaws hospital, which was followed by a typical yaw at the site after thirteen days.

Strange as it may seem, frambesia tropica is a disease more often acquired by the parent from the offspring, than vice versa.

HISTOPATHOLOGY

The skin lesions of the various so-called stages of frambesia tropica present the same histopathologic picture. The following is a summary by Macleod of his studies on yaw material from Ceylon:

I. Changes in the Corium
  1. Blood vessels: dilatation and tortuosity of those in the papillary and subpapillary layers; no thickening of the vessel walls or endothelial proliferation; vessels persist in the granuloma
  2. Cellular infiltration consisting of:
    (a) Plasma cell infiltration at first most marked in the neighborhood of the vessels, follicles, and glands, rapidly becoming diffused; no definite arrangement in rows; no large multinuclear cells; no tendency to organization detected
    (*b*) Marked extravasation of polynuclear leukocytes
  3. Fibrous stroma
    (*a*) Collagen attenuated where the granuloma is densest; no definite degenerative changes
    (*b*) Elastin similarly affected
  4. Hair follicles, sebaceous glands and oil glands seem healthy
II. Changes in the Epidermis
  1. Marked proliferation and down growth of the interpapillary processes so great in the older lesions as to resemble condyloma acuminatum
  2. Basal layer uninterrupted
  3. Edema affecting prickle-cells and interepithelial spaces
  4. Disappearance of pigment in the affected area
  5. Transitional layers imperfect
  6. Cornification marked hyperkeratosis and parakeratosis, with deposition of leukocytes and debris between horny lamellae

Sections from frambesia lesions stained by Levaditi's method discloses the *Spirochaeta pertenuis* in the region of the thickened interpapillary pegs of the epidermis.

POSTMORTEM FINDINGS

The disease is seldom fatal, hence opportunities for investigation are rare. Rake reported four necropsies at a leper asylum. In none of the patients did he find anything resembling the primary lesions of syphilis, nor were there any tertiary symptoms such as deep and obstinate ulceration with destruction of bone or gummas in the subcutaneous tissues or viscera. His fourth subject had a perforating ulcer, but this was probably due to the leprosy from which he was also suffering. No gummas in the connective tissue, muscle, periosteum or viscera were found.

SEROLOGY

The Wassermann test does not differentiate syphilis and frambesia tropica, because the latter is one of the diseases that gives the so-called paradoxical Wassermann or positive result in the absence of syphilis. Bates of Ancon Hospital, Canal Zone, reports nine cases, five positive (one partial) and four negative (method not given). Bloombergh, using the original Wassermann test, except for normal guinea-pig heart antigen, found two cases strongly positive. One of the cases was positive seven days after treatment (dose not mentioned) with arsphenamin. Dr. Gutierrez told me he had records of seven cases not all of which gave a positive Wassermann reaction. I had the Wassermann test performed on seven cases; they were all positive. In one case, a reversal of the Wassermann test occurred after three doses of arsenobenzol (Schamberg) had been given — dosage total, 10 decigrams. This patient, whom I was able to keep under observation for almost a year, remained persistently negative and asymptomatic.

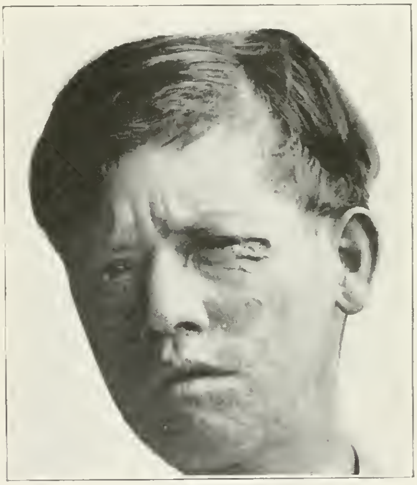

Fig. 4.—Lesion at mucocutaneous angle of secondary stage of frambesia tropica. (From report of commissioner of health, Porto Rico.)

ANIMAL INOCULATION

Monkeys can be successfully inoculated from human cases. The experimental incubation time varies between 16 to 92 days. In the lower species of monkeys, a local lesion only follows, but the blood is infectious, and injections of blood give rise to other local lesions if further inoculated. Monkeys can also be inoculated from the serum of lesions from monkeys. The orangutang has shown generalized frambesia four months following local inoculation.

Rabbits are also inoculable, and as in syphilis, the testicle and the scrotum have been successfully inoculated.

TREATMENT

The old treatment was tedious and well nigh fruitless. Mercury was without result. Potassium iodid, unless given in large enough doses to produce iodism, did not heal the lesions. Arsphenamin and neoarsphenamin with their modifications—novarsenobenzol, novarsenobillon, arsenobenzol, arsenobillon and kharsivan (B. & W.)—given either intramuscularly or intravenously have revolutionized the therapy. Brochard recommends rectal injection, especially in young children. The results of arsphenamin are evident within from a few days to a fortnight. Most writers seem to consider that the "therapia sterilisans magna" of Ehrlich is feasible in frambesia tropica. Recurrence after single injections have been reported only when small doses were administered. In one series of cases, equal but not equivalent doses of arsphenamin and neoarsphenamin were followed by recurrence only among those receiving the smaller neoarsphenamin dosage.

During the war shortage of arsphenamin, Castellani continued his earlier experiments on a curative mixture, with the following result:

Castellani's Yaws Mixture (Modified)

℞	Tartar emetic	gr. i
	Potassium iodid	ʒ i
	Sodium salicylate	gr. x
	Sodium bicarbonate	gr. xv
	Glycerin	ʒ ii
	Aqua q. s. ad	℥ i

An ounce of the mixture is given three times a day diluted with three or four times the amount of water to adults and children over 14; half doses are given to Europeans and children between 8 to 14. The medication is continued for from ten to fifteen days, remitted for one week, and then give again for from ten to fifteen days.

Tartar emetic intravenously is beneficial but slow.

The local treatment consists of cleanliness, antiseptic solutions or salves, or iodoform.

The prognosis, especially with modern therapy, is good. Complete cures are the rule. The disease is apparently more severe in children, and secondary infection may cause trouble.

Some observers note reinfection following arsphenamin cures. Among aboriginals, it was common to infect all the young children with yaws so that they would not get it later. It has been asserted that this vaccination frambesia was a modified and less virulent form.

Experimentally, frambesia is apparently auto-inoculable, and hetero-inoculable when the rash is still present. One of my patients, referred to above, inoculated himself on the foreskin during the generalized period.

PROPHYLAXIS

The prophylactic measures consist in isolation in special yaws hospitals in infected districts. Each patient should be covered with a mosquito bar to prevent the access of flies to the wounds. There should be compulsory notification of cases in places where health boards are established, and immediate treatment with arsphenamin or its modifications should be instituted.

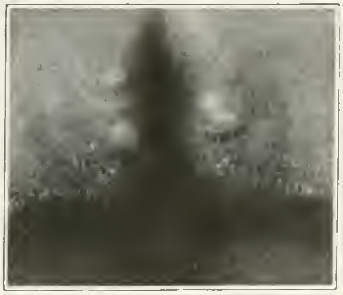

Fig. 5.—Mother yaw and satellites in intergluteal fold. (From report of commissioner of health, Porto Rico.)

Those who may accidently become contaminated with the secretion from frambesia lesions should use the so-called early treatment, wash with soap and water, and apply a mercurial.

Rarely has the disease been acquired through sexual intercourse. Among over 900 prostitutes, I found but five active cases of frambesia; 12 per cent. of these women presented active lesions of syphilis.

The disease seems to remain in certain houses or schools, and the demolition of these has been practiced.

FRAMBESIA TROPICA AND SYPHILIS

The identity of syphilis and yaws has been affirmed and denied innumerable times. Prior to the discoveries in bacteriology and serology of this century, scientific gentlemen in different parts of the tropical world amassed a huge fund of clinical differentiation. The accompanying tabulation from Jeanselme and Rist (quoted from Butler's article) gives many of the points that lead most observers to maintain the dual character of these diseases:

Comparison Between Syphilis and Frambesia Tropica

SYPHILIS	FRAMBESIA TROPICA
1. Disease pandemic	1. Disease tropical
2. Acquired by heredity and contagion	2. Acquired only by contagion
3. Begins by a primary pathognomonic lesion at point of inoculation	3. Initial lesion near portal of entry is not constant nor different from lesions appearing later
4. Immunity conferred by syphilis is in a sense permanent	4. Reinoculation of yaws is possible
5. All attempts at autoinoculation of a patient with secondary or tertiary syphilis are fruitless.	5. The autoinoculation of yaws is possible for an indefinite period, but quite long
6. The hard chancre and other signs of syphilis can appear on a subject who may have yaws	6. Yaws can develop on a subject with syphilis
7. The polymorphism of syphilitic manifestations	7. Monotony of eruption; it showing only papilloma
8. Syphilids, at least those of the tertiary period destroy the skin, and leave after cure, permanent scars	8. Frambesial lesion which is not exposed to any irritation heals without leaving a trace
9. Syphilis is an infection in which the several lesions correspond to three periods, primary, secondary and tertiary	9. All the manifestations of yaws are identical, whatever be their date
10. Syphilitic eruption involves mucous membranes	10. Frambesia lesions do not involve mucous membranes
11. Localizations in the viscera	11. No localization in the viscera
12. Syphilids are not pruriginous	12. Yaw lesions are accompanied by lively itching
13. Alopecia in secondary period	13. No alopecia in the course of the disease

Manson mentions the following points of contrast in the clinical features of the two diseases, all of which are lacking in frambesia tropica: primary sore; infection of fetus; adenitis; exanthem; alopecia; absence of itching; iritis; affection of the permanent teeth; bone and eye affections; congenital lesions; polymorphism of the eruption; nerve lesions and gummas of syphilis. Moreover, both diseases may occur in the same individual.

Macleod on the histologic examination gives this summary which suggests that frambesia tropica and syphilis are different histologic entities.

(*a*) Cellular infiltration. The plasma cells are not so definitely clustered around the vessels in yaws as they are in syphilis, nor do they ever form foci suggesting a tuberculous nodule, as they occasionally do in the latter disease. They are seldom arranged in rows, which frequently occurs in syphilis. Large multinuclear cells (chorioplaques) and true giant cells which may be present in syphilis are absent. No hyaline degeneration, such as may be found in syphilis, is detected in the plasma cells.

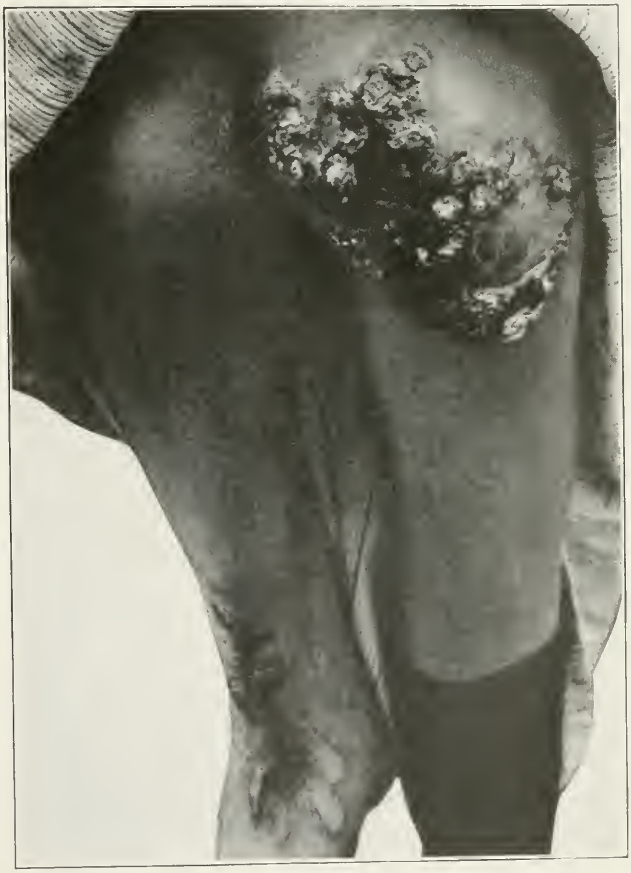

Fig. 6.—Ulcerating lesions of secondary stage of frambesia tropica. (From report of commissioner of health, Porto Rico.)

(*b*) Fibrous stroma. The rarefication of the collagen is more marked in yaws than in syphilis; organization is not detected, and colloid degeneration such as occurs in syphilitic gumma, is absent.

(*c*) Blood vessels. There is no tendency to thickening of the vessel wall, or to endothelial proliferation, such as so frequently pertains in syphilis.

(*d*) Epithelium. The proliferation changes in the epidermis in yaws are only equalled in syphilis in the condylomata, while the marked tendency of the stratum corneum (hyperkeratosis), which is an invariable characteristic in yaws, is unusual in syphilis.

Maul from a roentgen-ray examination of twenty cases notes

> That with the exception of 2 per cent. of cases showing as a swelling over the surface of bone, the roentgen-ray picture is different from the bone lesion of syphilis in that:
>
> (1) The periosteal infiltration is absent.
>
> (2) The thickening of the cortex of the bone is absent. Also in the 2 per cent. of cases where thickening of the cortex is present, the thickening remains localized, does not extend along the whole length of the bone, and sooner or later shows rarefication in the center of the bone.
>
> The radiograph can be used as an additional means of differentiating yaws from syphilis, where there is involvement of the bone, and as a confirmation of the evidence that the two diseases are distinct.

Diagnosis by therapeutic agents in the case of mercury may be of slight aid, since mercury has little if any effect on the lesions of frambesia. The results of specific chemotherapy are equally good in syphilis and in yaws, although it is maintained that the latter disease proves more amenable to arsphenamin.

The demonstration, almost simultaneously, of the causative organism in both diseases did not furnish conclusive ground for differentiation. The spirochetes, pallida and pertenuis, are morphologically identical, and biologically very similar. However, the following differences in experimental infection of frambesia tropica compared with syphilis have been noted by Nichols:

> Incubation period for testicular lesion is eight days shorter, and for skin lesions it is twenty days shorter (in frambesia).
>
> Lesions of yaws can be cured with smaller doses of salvarsan.
>
> Serum reaction does not appear as promptly.
>
> Syphilitic rabbits treated with salvarsan can be infected with yaws fourteen days after treatment, while reinfections with syphilis do not occur under the same circumstances.

Advances in immunity and immunity reactions have been of some help in maintaining the dual character of these diseases. Patients with syphilis can be inoculated with frambesia, and respond with the lesions of yaws. Patients with yaws may be inoculated with syphilis and pass through typical primary and secondary syphilis. Frambesia is auto-inoculable and hetero-inoculable even in the secondary generalized stage of the disease. Once the syphilitic spirochete has advanced beyond the local site of inoculation, neither auto-inoculation nor hetero-inoculation will succeed.

Serologic diagnosis proved of no aid in the subject, for both diseases excite a reaction in the blood of the patient that gives a Wassermann positive result. Castellani at one time believed that the antigen bodies in both diseases were different, but the later discoveries of the nonspecificity of antigen in the Wassermann test has made negative any distinction.

That frambesia tropica is not transmitted from the infected parents, no matter in what period of the disease they may be, to the offspring during the intra-uterine existence of the fetus is a strong argument in favor of nonidentity. Hereditary syphilitics do not acquire syphilis, yet I have seen a case of generalized frambesia in a typical hereditary syphilitic boy, who had the typical Hutchinson triad, notched spade upper incisors, marked iritis and deafness.

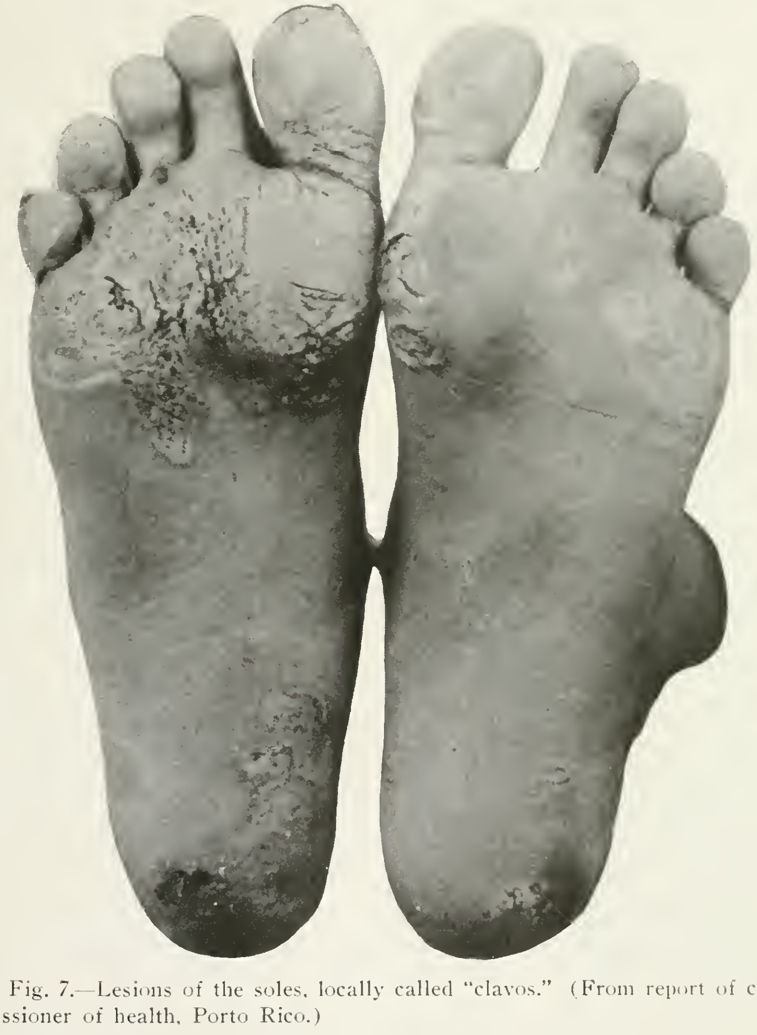

Fig. 7.—Lesions of the soles, locally called "clavos." (From report of commissioner of health, Porto Rico.)

The mother of an hereditary syphilitic child does not acquire syphilis from her offspring, but it is a common observation that an infant with yaws infects its mother. The location of the primary yaw on the nipple, and over the ilium, where the native mother carries her baby, is evidence of this.

My own clinical observations in the tropics, where I was in the position to observe all the skin diseases among upward of 20,000 native men and women for fourteen months, do not incline me to the theory that frambesia tropica is a modified form of syphilis. The syphilitic eruptions I have seen among these people were in no way different from the same type of eruption encountered in the temperate climes. Contrariwise, the clinical appearance of the frambesia cases appealed to me as having an individuality not imitated by the generalized syphilitic eruptions. The bright red moist granuloma underneath the dry yellow crust should distinguish this affection.

For the presentation of the characteristics these diseases have in common, I refer the reader to Captain Butler's [1] paper, "Some Facts and Fancies Regarding the Unity of Yaws and Syphilis."

SPECULATION

The theory that frambesia tropica is a form of syphilis changed by climatic conditions and by centuries of passage through the colored race has been advanced. The possibility of the transmutation of the spirochete may be reserved. Certainly, our present knowledge on transmutation of bacteria is too meager to warrant its discussion.

SUMMARY

Frambesia tropica exists in our nearby southern neighbors, Porto Rico and Panama, with whom we are having an ever increasing commercial and social relationship. As it exists in these places, where I had the opportunity to study ten examples of the disease, it corresponds to the descriptions given under various other names in other parts of the tropics and subtropics. I demonstrated the *Spirochaeta pertenuis* and I corroborate the finding that this organism is morphologically indistinguishable from *S. pallida*. The serology was investigated and all the cases gave positive Wassermann reactions. Five cases were diagnosed among upward of 900 prostitutes.

I could not make the diagnosis of tertiary yaws, on the presence of ulceration or scarring. One case was in an hereditary syphilitic child presenting a full fledged frambesia eruption, and the Hutchinson triad.

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1. Butler: Some Facts and Fancies Regarding the Unity of Yaws and Syphilis, U. S. Naval Med. Bull. **8**:561, 1914.

Treatment with arsenobenzol (Schamberg) and novarsenobillon in my hands has given the beneficial results described by others.

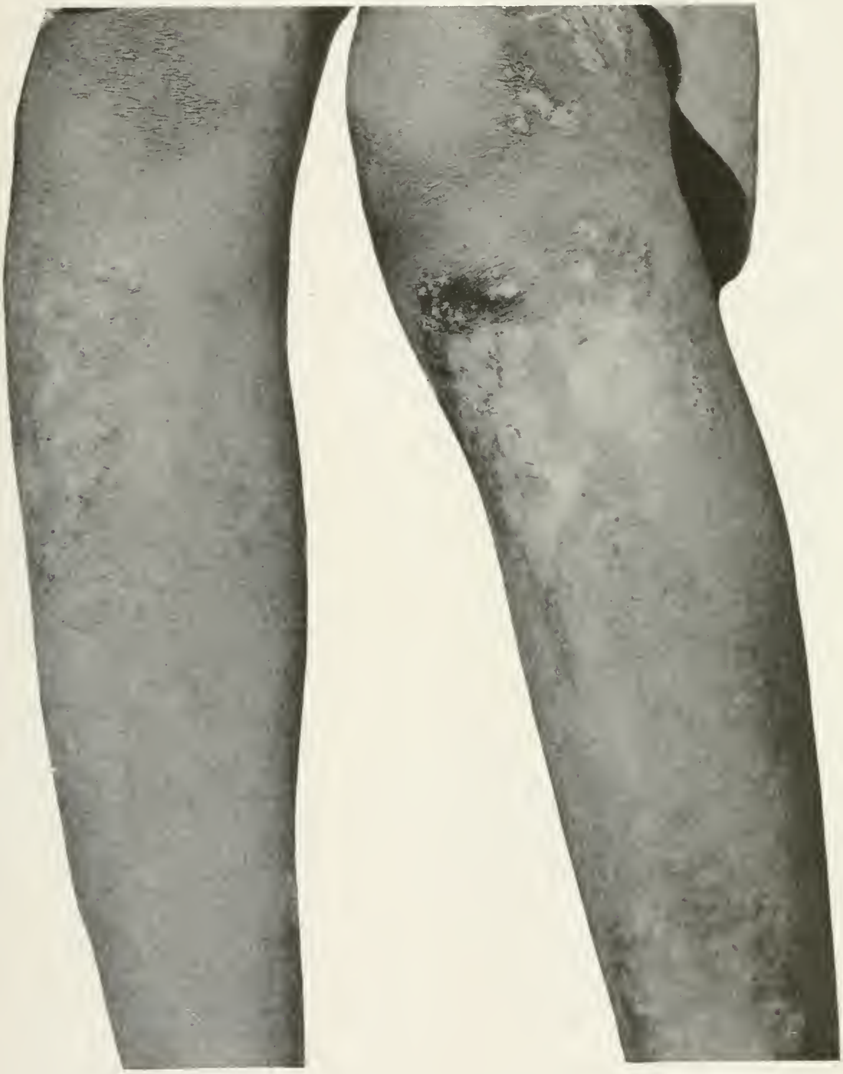

Fig. 8.—Ulcerating lesions with loss of substance followed by scarring. (From report of commissioner of health, Porto Rico.)

Personally, I am inclined to the belief in the dual character of frambesia tropica, and syphilis on clinical grounds alone. The extensive evidence accumulated is confirmatory to nonidentity.

Thanks are extended to the gentlemen of the laboratory of the Institute of Tropical Medicine and Hygiene, San Juan, Porto Rico; of the Department of

Health, Porto Rico; and to the Santo Tomas Hospital, Panama, R. P., for aid in the technical studies.

My own photographs, taken with a kodak, were not clear enough for reproduction, and I especially thank Dr. J. Lugo Viña, Secretary, Board of Health, Porto Rico, for his kindness in supplying me with the photographs taken by his department of cases of a recent epidemic.

15 Central Park West.

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XIII.—MULTIPLE BENIGN CYSTIC EPITHELIOMA ASSOCIATED WITH XERODERMA PIGMENTOSUM *

SANFORD M. WITHERS, M.D., AND WILLIAM G. COLEMAN, M.D.
ST. LOUIS

In reviewing the extensive literature dealing with these diseases, one is impressed with its complexity, the confusion of terms and the diversity of types of lesions. There are four points of similarity between the two conditions: (1) the hereditary tendency; (2) the unknown etiology; (3) the age incidence, and (4) the appearance of lesions, chiefly on the exposed parts of the body, consisting of atrophic cutaneous changes, pigmentation and multiple carcinomatosis.

Benign cystic epithelioma (Brooke) may be defined as a circumscribed cutaneous atrophy and relatively benign carcinomatosis of unknown etiology and definite hereditary tendency, occurring in early life on the exposed portions of the skin, notably the face and hands, characterized by the formation from tiny pigmented papules, or of firm, raised, semitranslucent, pinkish, tubercular or nodular, flattened masses that show no tendency toward involution.

Brooke,[1] in 1892, separated this condition from other adenoid skin epitheliomas and his observations have been confirmed by Fordyce,[2] Unna, Stelwagon and others. Adamson,[3] in 1908, attempted to point out the differences between this condition and multiple rodent ulcer, which "led to the query that has not been answered, 'as to what is the essential difference between a benign and a malignant epitheliomatous growth.' "

Xeroderma pigmentosum (Kaposi) is, by definition, a disease of low malignancy and unknown etiology, developing in early life and tending to occur in many members of the same family. The chief characteristics are: precociously senile cutaneous changes, pigmentation and carcinomatous metamorphosis affecting exposed portions of the skin.

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* Studies, reports and observations from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine. Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

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Hebra and Kaposi [4] first described the condition as a clinical entity in 1870, and Kaposi gave detailed histories and pathologic findings in 1882. Since that time over 200 cases have been reported, more than eighty of which have been studied thoroughly with almost as many theories as to etiology and mode of origin — but these reports seem to have added little to the knowledge of the subject.

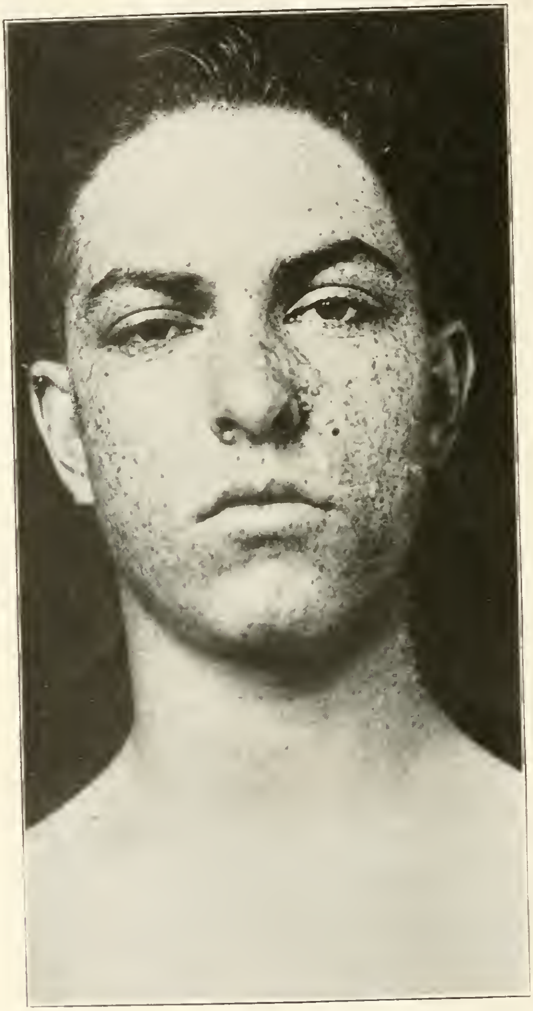

Fig. 1.—May, 1919. Showing distribution of lesions, scarring from previous treatment and tumors, the smaller ones deeply pigmented, some pearly, vesicle-like, others ulcerated, crusted. On the right cheek just anterior to the ear can be seen the suture line of the second biopsy.

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[4] Hebra and Kaposi: Lehrbuch der Hautkrankheiten, 1870.

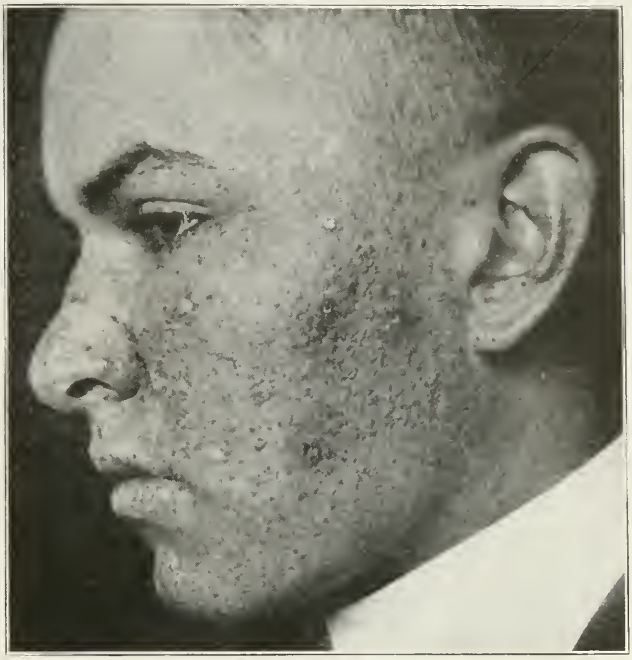

Fig. 2.—Aug. 3, 1919. Note small pigmented areas and tumors of ear.

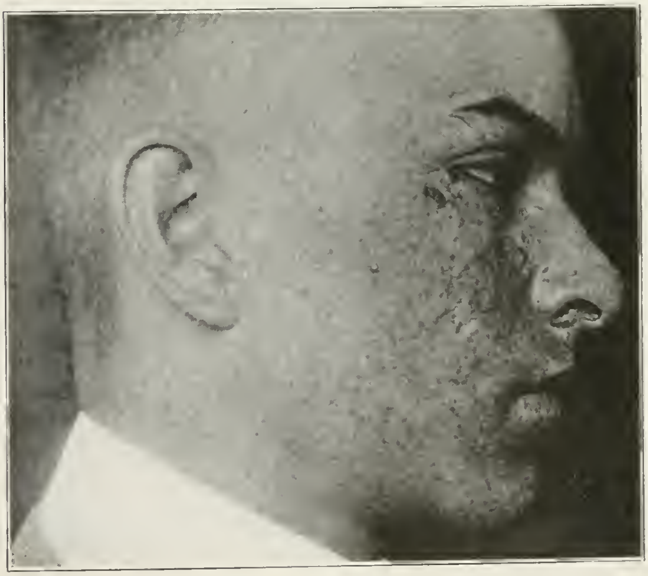

Fig. 3.—Aug. 3, 1919. Note small pigmented areas and tumors of the ear, also single, deeply pigmented growth near outer angle of right eye.

The histopathology, as reported by Kaposi, Taylor,[5] Unna, Pollitzer,[6] Councilman,[7] McGrath [7] and Stelwagon shows many associated conditions, such as sarcoma, myxoma, angioma and granuloma — but the predominating feature is epithelioma, which may be of the prickle or of the basal cell type (Kreibach, Pernet, Halle [8]). They are often pigmented, as in sailor's carcinoma (Unna).

Xeroderma pigmentosum has been divided into two distinct clinical types — the early malignant condition which results in death before adult life, and the delayed or late dermal atrophy associated with benign carcinomas.

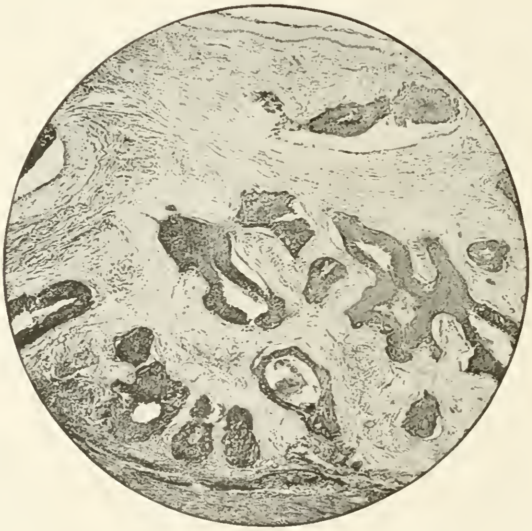

Fig. 4.—Low power. Biopsy No. 1, January, 1919. A nodule recurrent at the border of a scar left by previous caustic treatment. This section shows embryonal epithelial cells arranged in cords, masses and alveoli enclosing homogeneous eosin staining material, surrounded by a subdermal layer of scar tissue below a thinned epithelium.

The case we report is one of undisputed xeroderma pigmentosum, clinically, which is associated with a frank and characteristic multiple benign cystic epithelioma. It does not fall, then, into either the juvenile malignant or late benign class, and is, therefore, unique in that it has been present from the patient's earliest recollection and has not become malignant. This patient may be in a transition stage between the two fairly distinct types.

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REPORT OF A CASE

Family History.—L. S., aged 18, a young white man, American born of German parents, had a negative family history for similar conditions, save that the mother died of "cancer" at the age of 45 and the brother "freckled" easily. The freckles were removed by some local application at an early age and have not returned. The parents, brother and sister are of a pronounced brunette type.

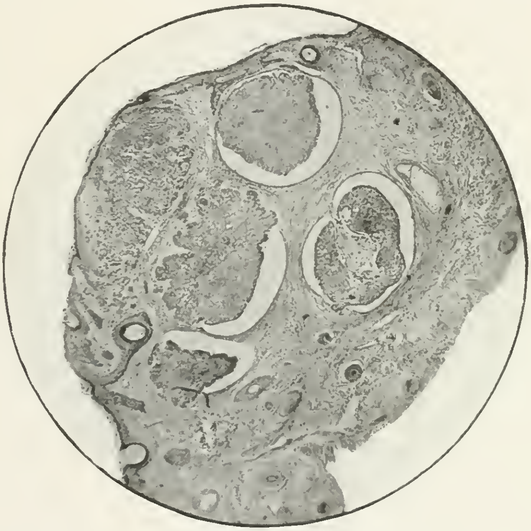

Fig. 5.—Low power section of small, deeply pigmented lesion just anterior to right ear. Biopsy No. 2. This section shows elevation of tumor from surrounding fairly normal skin. Direct connection of the basal layer of the epithelium with the masses of similar cells situated in the dermis is shown as well as finger-like projections also from the basal layer. Four definite, cystic structures are seen, with lining membrane surrounding homogeneous colloid-like material into which projects a bud of massed basal epithelial cells arranged about a scanty stroma connected with the dermis. The lining membrane of each cyst is reflected about the papillomatous structure except at its pedicle.

Past History.—The patient was born and reared in the city The only serious illness was measles, without complications, at the age of 8 years.

Present Illness.—The patient stated that as far back as he could remember, his face, neck and hands had been covered with "black freckles," as well as a few on the ears. Because freckling occurred so readily when exposed to sunlight, he was kept in the house and later chose indoor work. For the last few years he has been employed at night. When 14 years old he noticed "a small, hard, lumpy" tumor on the left side of the nose which grew to the size of a pea and was removed with "the electric needle." At this time similar shiny tumors appeared on the cheeks, nose, forehead and eyelids, eighteen of which were treated with "acid," causing the disappearance of a few, but most of them recurred in the scar. More continued to appear. Many local applications of salve were made, but with no benefit. The patient refused roentgenray treatment. Since the age of 15 there had been successive crops of small tumors developing over the face, chiefly in spring and summer. Some of these had undergone ulceration, and many had completely disappeared under treatment with caustics, excision and thermocautery. Biopsies were made in January and May, 1919.

Physical Examination.—The patient was a well developed, well nourished young man with no gross abnormality. The hair was reddish-brown; the eyes were brown; and the skin on the exposed portions of the body had a swarthy appearance. Over the forehead, face, ears and neck, extending below the clavicle anteriorly and to the seventh cervical vertebral spine posteriorly were many lentiginous spots varying in size from 1 to 4 mm. Similar spots appeared on the dorsum of the hands. There were many white, irregular scarred areas on the face up to 1 cm. in diameter, some of which were covered with a fine scale. The skin of these areas, particularly of the face, was rugose, dry, thickened and somewhat immobile. Intermingled with these scars were numerous tiny tumors from 0.5 to 10 mm. in diameter, scattered irregularly over the face. Some of the larger ones were ulcerated in crater form, covered with dry, hemorrhagic crusts, and had pinkish, pearly, raised margins; others were dull red in color, semitranslucent, almost vesicular in appearance and

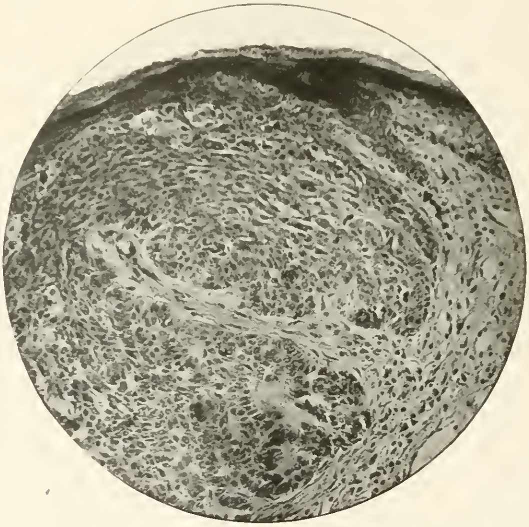

Fig. 6.—This high power section from Figure 5 shows the direct connection between the epithelium and the mass of epithelial cells below. The cells are not infiltrating, but invading behind a basement membrane, and the rapid proliferation is shown by the two mitotic figures. The small amount of stroma is made up of young connective tissue and thin walled vessels about which there is a moderate small round-cell infiltration.

raised from 1 to 3 mm. The surface was glistening and about the periphery could be seen many tiny dilated venules. The smaller tumors, from 1 to 3 mm. in diameter, were dark-brown to black in color and were raised a little above the surrounding skin. Pressure on a tumor produced a dull pain. Fluid was not expressed on pricking the skin. The condition of the teeth was poor; there was a decayed upper molar. There were no palpable glands in the neck. The remainder of the physical examination was negative. Blood pressure averaged about: systolic, 120; diastolic, 80.

Blood examinations from time to time averaged: Red blood cells, 5,472,000; white blood cells, 8,200; hemoglobin, 85 per cent. Differential, 500 cells: neutrophils, 53 per cent.; basophils, none; eosinophils, 1 per cent.; small lymphocytes, 42 per cent.; mononuclears and transitionals, 4 per cent. No abnormal cells were seen at any time

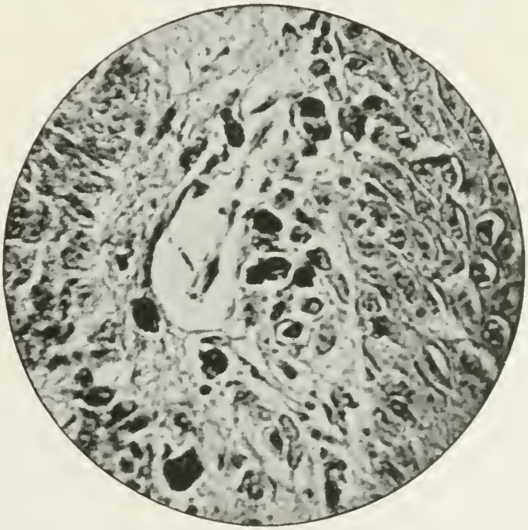

Fig. 7.—A higher magnification of an area of Figure 5 to show the occurrence of irregular masses of dark-brown pigment within the stroma of islands of epithelial cells. These pigment deposits are found in the neighborhood of large thin-walled vessels.

This case then presents the following characteristics of xeroderma pigmentosum: It began in early life and became progressively more pronounced. It now presents clinically: scarring, hyperkeratosis, telangiectases, brown and black pigmentation, and epitheliomas on exposed portions of the skin. The blood shows an oligocythemia and relative lymphocytosis with slightly diminished hemoglobin, as found by Okamura.

Histology.—Histologically there occurs an acanthosis and parakeratosis intermingled with a thickening of the corium and thinning of the epidermis. The corium shows a fairly marked, small round cell infiltration, and an increased proliferation of blood vessels around which there are large masses of dark pigment.

Pathology.—The pathologic picture is that of multiple epitheliomas. The masses of cells show numerous direct connections with the basal layer of the epidermis and are supported by scanty stroma. The individual cells are of the embryonic basal type, rapidly proliferating with many mitotic figures, but showing no tendency to break through the basement membrane. The many tiny cysts have projecting into them intercystic papillomatous masses of epithelial cells from which the limiting membrane is reflected to form the lining of the cavity which is partly filled with homogeneous colloidal material. The histopathology, therefore, is that of multiple benign cystic epithelioma associated with xeroderma pigmentosum.

Treatment.—The only treatment given this patient aside from excision of tumors for biopsy was the application of a radium plaque to fourteen of the larger lesions. This caused them to disappear in three or four weeks, leaving smooth pink scars. We were unable to keep the patient under observation as he insisted on leaving the city.[9]

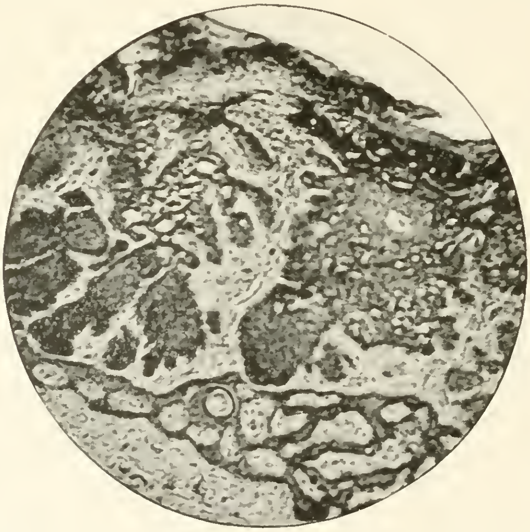

Fig. 8.—Also high power of Figure 5. An area at the surface overlying down growths of epithelial cells, showing degeneration with the formation of vacuoles and tiny vesicles. Some cells have undergone dissolution. The area is edematous and there is marked round-cell infiltration throughout.

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9. In addition to the references given, the following will be found of interest:

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ONYCHAUXIS DUE TO HYPOPITUITARISM

LESTER HOLLANDER, M.D.
PITTSBURGH

In burdening the literature with this case report, I find my justification in the complex picture presented by this patient.

REPORT OF CASE

The patient, R. D., was referred to me by Dr. J. W. Boyce on account of the peculiar formation of his fingernails. This formation had existed practically since his birth, with constantly progressive changes. The nails appeared to show a hypertrophy in breadth and thickness, and were changed in color, texture and density.

All nails were involved, though the process originally started on the nails of the great toes, and gradually involved all of the toes and fingers. The most marked changes were noticed in the nails of the great toes; these were much thicker than normal, and the upper surface was grooved by the uneven piling up of nail substance, giving them a transversely striated appearance. The grooves could be distinctly felt and gave the nails a rough feel. The nails were lusterless and were brown, dark brown or black; the older the involvement the darker the color of the nail.

Family History.—The father and mother were alive and well. The patient was the youngest of four children. The other two were 24 and 22 years, respectively, and one was stillborn twenty years ago. There was no conception after this stillbirth, until the birth of the patient, who was 9 years old. There was no conception after his birth. The patients' mother's aunt died of pulmonary tuberculosis. There was no family history of syphilis or heart disease.

Personal History.—The patient was of normal delivery, breast fed. Dentition began at 6 months. He began to talk at 12 months and began to walk at the age of 13 months. He had had measles and German measles. When I saw him he was 9 years old, and was in the third grade of the public school and getting along fairly well in his studies. For the last six years he had been suffering from a dry cough which was brought on particularly by exercise. No medication appeared to affect it, nor were any seasonal differences noted. The cough did not seem to incapacitate him or in any measure to interfere with his welfare. He had frequent attacks of ulcers on the tongue and the buccal mucous membranes. These ulcers, which were bright red, slowly turned to grayish white and disappeared spontaneously. This condition also was of about six years' duration.

The patient had an abnormal appetite and ate ravenously and frequently; as his mother expressed it, he "could eat all the time." He had frequent attacks of nausea followed by vomiting; these always occurred at night and were followed by severe headache of a migraine type. The color of the vomitus was usually dark brown. These attacks were of three year's duration and were progressively becoming more frequent. He complained of difficulty in vision at times, with considerable blurring of letters. He was also troubled with occasional "spells." He went into a subconscious state from which he was roused with difficulty (petit mal). I observed one of these, and it was typically epileptiform.

Physical Examination.—The patient was a well built boy of larger height than the average, light complexion, well nourished and active and intelligent. He weighed 33 kilograms.

The head was normally formed; the hair was blonde and dry; the eyebrows were highly arched and scanty in growth. Pupillary reaction was normal. The palate was highly arched. The teeth showed a slight edging and many were decayed. The tonsils were greatly hypertrophied and the follicles were filled with debris. A fairly pronounced formation of breast structure with a good deal of erectile tissue in the nipples gave the chest a feminine appearance. There was a distinct tenderness in the left lumbar region.

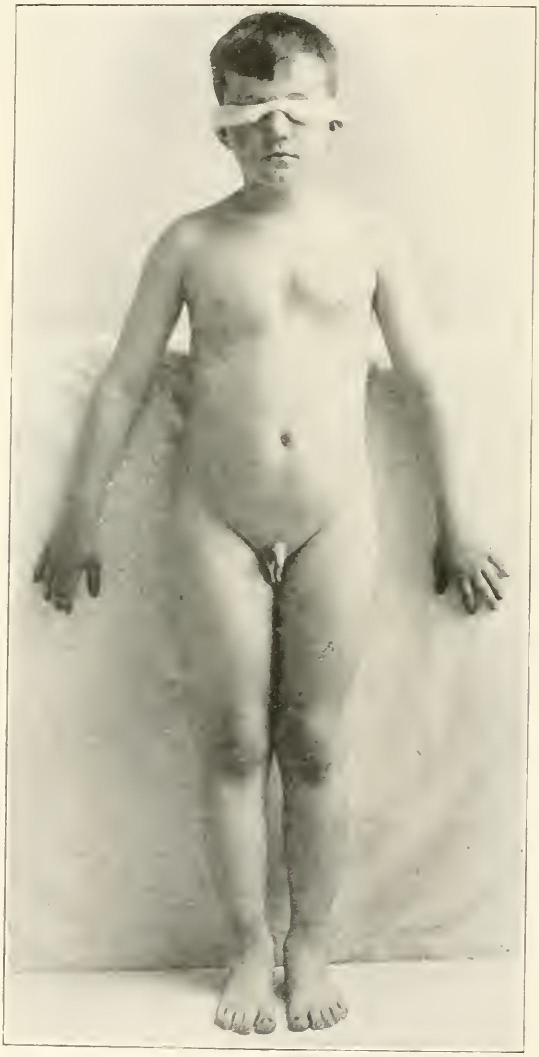

Fig. 1.—Breast structure, broad pelvis and small genitalia.

The pelvis was broad and feminine in appearance; mons veneris was pronounced. The measurements of the pelvis were: External conjugate diameter. 12.5 cm.; interspinous conjugate diameter, 16.0 cm.; intercrestus conjugate diameter, 19.0 cm.; left external oblique diameter, 15.0 cm.; right external oblique diameter, 15.0 cm., and bitrochanterie diameter, 23.5 cm. The reflexes — patellar and biceps — were almost entirely absent. Genu valgum was quite noticeable.

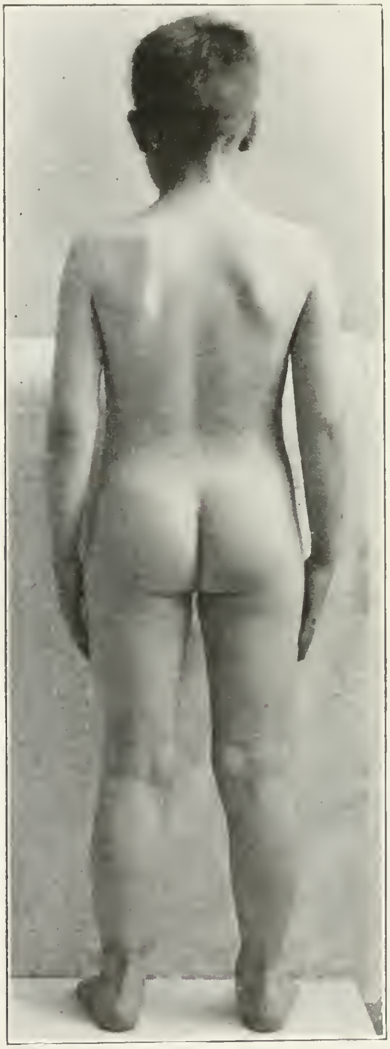

Fig. 2.—Marked feminine hips and genu valum.

Special Examinations.—Eye Examination: Vision, right eye, 16/40; left eye, 16/40. Mydriasis was produced by homatropin. The media were clear. Fundi: Partial (beginning) optic. There was atrophy in both eyes. Visual Fields:

There was slight contraction for white in the right eye and marked contraction up and in the left eye.

Roentgen-Ray Examination: Chest examination was negative (for enlarged thymus). The skull showed a small sella turcica; the anterior and posterior clinoid processes were very thick. The luetin skin test and the von Pirquet tuberculin skin test were negative.

Urinalysis: April 13, 1920: Color, amber; reaction, acid; specific gravity, 1.030; albumin, negative; sugar, negative; indican + +; microscopic, phosphates, amorphous mucous leukocytes.

April 15, 1920: Color, amber; reaction, acid; specific gravity, 1.030; albumin, negative; sugar, negative; indican, + +; microscopic, phosphates, amorphous mucous leukocytes.

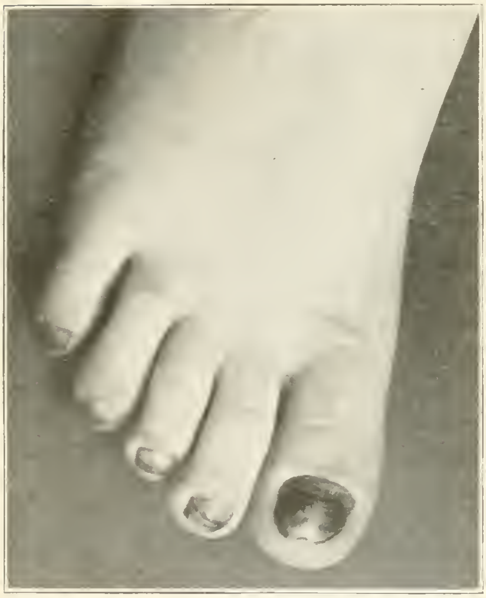

Fig. 3.—Appearance of toe nails.

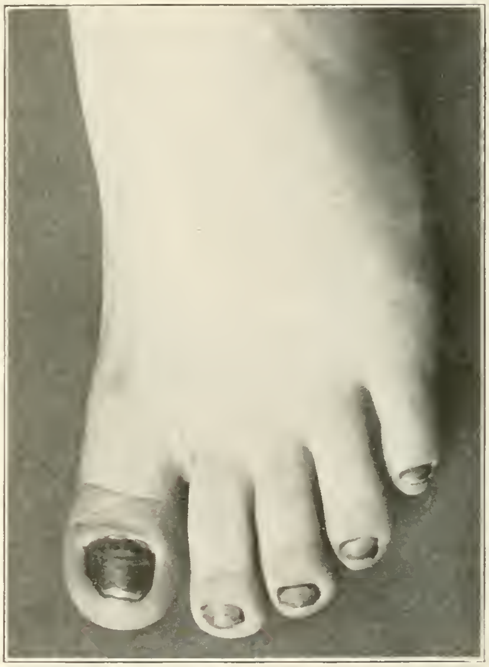

Fig. 4.—Appearance of toe nails.

April 17, 1920: Color, lemon; reaction, acid; specific gravity, 1.030; albumin, negative; sugar, negative; indican, +; white blood cells.

April 19, 1920: Color, straw; reaction, acid; specific gravity, 1.022; albumin, slight trace; sugar, negative; indican, —; same as above.

Blood Examination.—Cell count: April 12, 1920: Red blood cells, 4,960,000; white blood cells, 23,000; hemoglobin, 80 per cent. Talqvist; polymorphonuclears, 70 per cent.; small mononuclears, 25; large mononuclears, 3; transitionals, 2.

April 15, 1920: Whilte blood cells, 19,500; polymorphonuclears, 73 per cent.; small mononuclears, 22; large mononuclears, 4; transitionals, 1.

April 18, 1920: White blood cells, 13,800; polymorphonuclears, 76 per cent.; small mononuclears, 17; large mononuclears, 7; transitionals, 0.

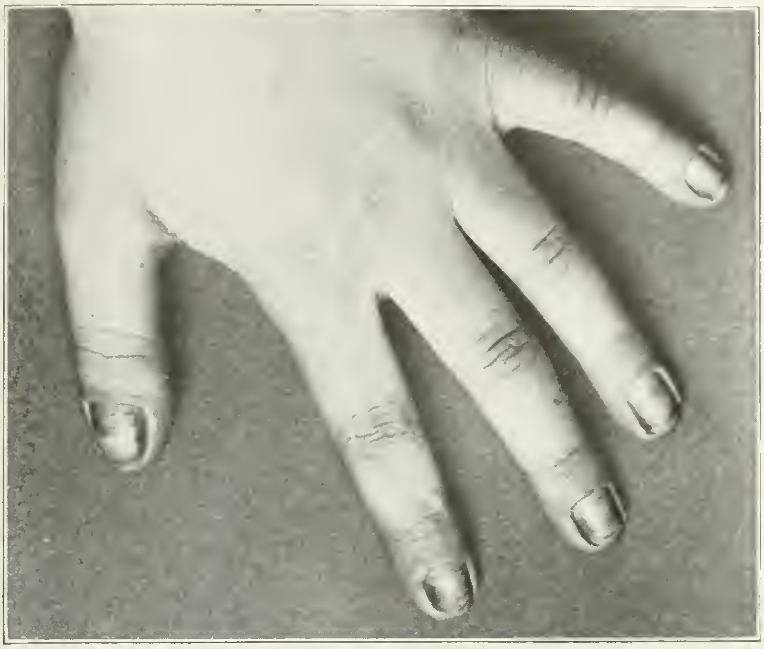

Fig. 5.—Appearance of fingernails; long, tapering fingers.

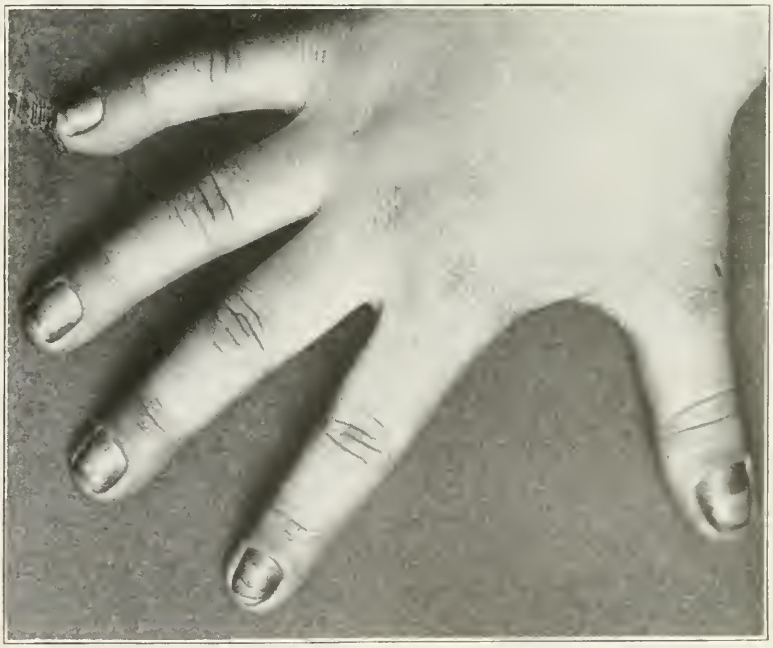

Fig. 6.—Appearance of fingernails; long, tapering fingers.

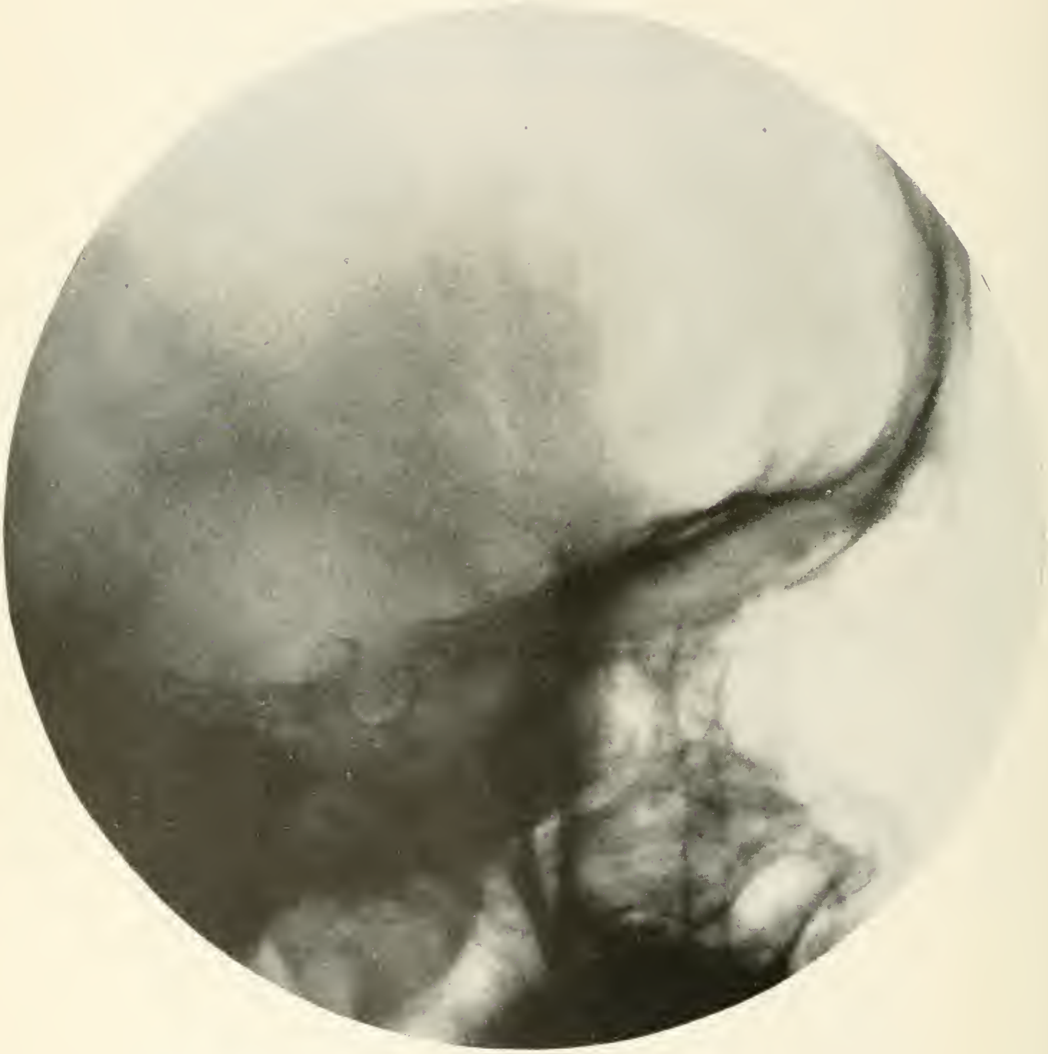

Fig. 7.—Roentgenogram of small sella turcica, thickened anterior and posterior clinoid processes; also thickened bony structure of base of skull.

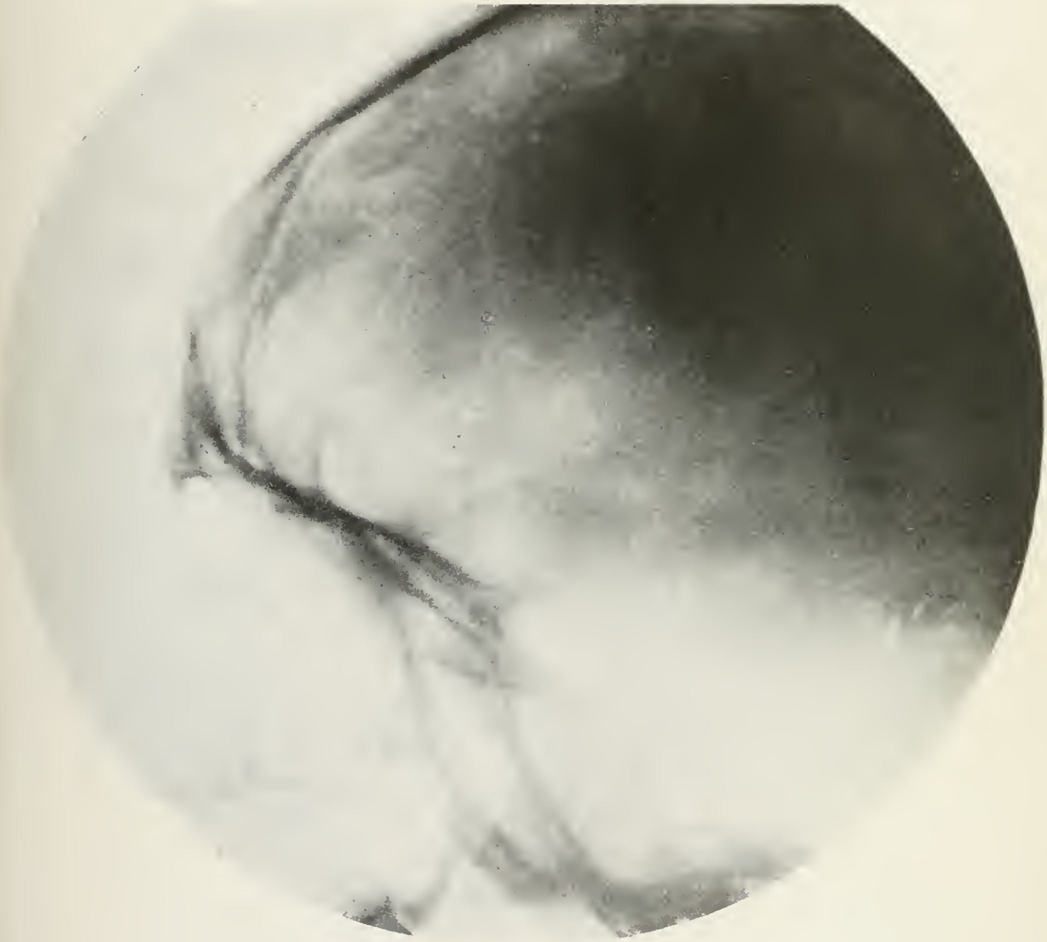

Fig. 8.—Roentgenogram showing marked difference in osseous structure of sella turcica and base of skull of normal 9 year old boy.

Complement Fixation Test: April 13, 1920: Cholesterinized antigen negative; acetone insoluble lipoid antigen, negative. Icebox: Cholesterinized antigen, negative; acetone insoluble lipoid, negative. The Goetch epinephrin test was negative.

On April 14, 1920, at 1:10 p. m., 66 gm. of glucose were given to find the patient's carbohydrate tolerance and a blood sugar test was made every half hour. The normal control was 0.36 per cent. The percentage of blood sugar at 1:40 p. m. was 0.34; at 2:10, 0.36; at 2:40, 0.42; at 3:10, 0.39; at 3.40, 0.36, and at 4:10, 0.36. The urine was also tested during this time every two hours for four successive tests, but no glycosuria could be elicited.

Spinal puncture and cystoscopic examination of the kidneys were not permitted by the parents.

DIAGNOSIS

The patient's general appearance, marked feminine character of the breasts and broad pelvis, slight suggestion of genu valgum, dry skin and hair, absence of signs of axillary or pubic hair, small genitalia, highly arched palate, enormous appetite, history of epilepsy (petit mal), frequency of and duration of colds (bronchitis), the appearance of the roentgen-ray findings, showing a small sella turcica with hypertrophy of the anterior and posterior clinoid processes, and his apparently high carbohydrate tolerance leads to the conclusion that this was a case of hypopituitarism, and that the trophic changes occurring in the nails may be safely attributed to this cause.

The optic atrophy, which the examination of his eyes revealed and which is likely to grow worse resulting in progressive failure of vision, is not due to his apparent hypopituitarism, and a trial of antispecific medication should be made.

His leukocyte count, so far unexplained, may be due to focal infection of tonsillar origin. Indicanuria and pain in the lumbar region are unexplained and for the present passed over as of less importance.

In a general way, with the exception of onychauxis, which was the cause of the investigation of this case, the case resembles very much a case described by Harvey Cushing.[1] His patient showed epilepsy, feminism, adiposity, overgrowth, suffering from colds, enormous appetite, sella turcica below normal size and an unusual solidity of the sphenoidal bone, broad pelvis, genu valgum, giving the body a feminine aspect, dry skin, no axillary or pubic hair, high carbohydrate tolerance and small genitalia. Our patient showed all these abnormalities in addition to the other signs described.

Cushing considers his case one of preadolescent dyspituitarism belonging to the group of dystrophia adiposogenitalis of the typus Frohlich, in which classification I believe the case under my observation may be included.

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[1] Cushing, Harvey: The Pituitary Body and Its Disorders, 1912; Case 34, p. 175.

TREATMENT

For treatment pituitary glandular feeding and antisyphilitic medication was advised.

ETIOLOGY OF ONYCHAUXIS

The etiologic factors entering into consideration of onychauxis are numerous:

Ormsby attributes them to local irritation from pressure, filth, neglect.

Pusey[3] states that enlargements may occur in acromegaly, that also in some cases they are due to developmental defects, or the result of circulatory disturbances.

Sutton[4] shows a very good illustration of onychauxis due to syphilis in Irwin C. Sutton's case.

Darier[5] considers the etiologic factors of all the onychoses under five distinct heads. This would also include onychauxis.

(*a*) Congenital malformations.
(*b*) Local causes, traumatism, parasitic affections.
(*c*) Localization of various dermatoses.
(*d*) Effect of general disease.
(*c*) Trophoneuroses.

In placing this case in the group of trophoneuroses due to hypopituitarism, I have not lost sight of the fact that there may be an hereditary syphilitic element and focal infection, but the presence of syphilis or focal infection could not be clearly demonstrated, while the evidence in favor of hypopituitarism is seemingly overwhelming. The entire clinical picture presented might possibly be cleared up if the presence of syphilis could be satisfactorily demonstrated.

I wish to express my gratitude to Drs. John W. Boyce, Adolph Krebs, George W. Grier and William H. Mayer for their cooperation in establishing this diagnosis.

7133 Jenkins Arcade.

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2. Ormsby: Diseases of the Skin, Philadelphia, Lea & Febiger, 1915, p. 1100.

3. Pusey: Principles and Practice of Dermatology, New York, D. Appleton & Co., 1917, p. 1187.

4. Sutton: Diseases of the Skin, St. Louis, C. V. Mosby Co., 1917, p. 864.

5. Darrier, T., and Pollitzer: Textbook of Dermatology, Philadelphia, Lea & Febiger, 1920, p. 431.

INTRASPINAL TREATMENT IN NEUROSYPHILIS

JAMES HERBERT MITCHELL, M.D.

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More than six years have elapsed since Dr. Oliver S. Ormsby and the writer instituted intraspinal therapy in our cases of neurosyphilis. Sufficient time, therefore, has passed to justify a survey of the clinical and serologic results obtained by this form of treatment.

LITERATURE ON THE SUBJECT

Many criticisms, notably those of Sachs [1] and of Dercum,[2] have been directed against intraspinal therapy on the ground that no clinical results can be obtained by the introduction of arsphenamized serum into the spinal canal, because it can be demonstrated experimentally that substances injected subdurally cannot penetrate the cortex of the brain, and that changes in the spinal tissue are beyond the reach of remedies in solution in the spinal fluid. Sachs firmly believes that sufficiently intensive intravenous medication will accomplish all that intraspinal therapy will accomplish. That arsenic appears in appreciable quantities in the fluid after intravenous injections of arsphenamin has been demonstrated by a number of workers, but the early work of Weed [3] and of Frazier [4] seemed to prove that dyes injected intravenously penetrated only the pial meshes, whereas dyes injected intraspinally penetrated not only the pial surfaces of the brain, but also the cortex.

Recently, attempts by Tzanck, Gilpin and Early, and by Barbat, have been made to increase the permeability of the choroid plexus for arsphenamin by spinal drainage after intravenous injection. Barbat [5] found that whereas only 31 per cent. of the cases punctured in twenty minutes after intravenous injection gave positive tests for arsenic, twenty-five out of twenty-six cases gave positive tests when the fluid was examined twenty-four hours after the injection. Hall[6] has endeavored to bring about a still greater permeability of the choroid plexus by the irritation of an intraspinal injection of the patient's serum preceding the intravenous injection of arsphenamin. It was found that intravenous injection of arsphenamin six hours after meningeal irritation by the injection of serum gave 92 per cent. penetrations and resulted in an average concentration of arsphenamin three times greater than that of the controls.

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[1] Sachs, B.: On the Intravenous, Not the Intraspinal, Use of Arsphenamin in Syphilis of the Nervous System, Arch. Neurol. & Psychiat. **1**:277 (March) 1919.

[2] Dercum, Francis X.: The Functions of the Cerebrospinal Fluid, with a Special Consideration of Spinal Drainage and of Intraspinal Injections of Arsphenamized Serum, Arch. Neurol. & Psychiat. **3**:230 (March) 1920.

[3] Weed, L. H.: Studies on Cerebrospinal Fluid. III. The Pathways of Escape from Subarachnoid Spaces, with Particular Reference to the Arachnoid Villi, J. Med. Res. **26**:51, 1914-1915.

[4] Frazier Charles H.: Cerebrospinal Fluid in Health and Disease, J. A. M. A. **64**:934 (March 13) 1915.

[5] Barbat, J. Henry: Permeability of the Meninges to Arsenic in Paresis and Tabes, J. A. M. A. **70**:147 (Jan. 19) 1918.

The addition of a solution of neo-arsphenamin directly to the spinal fluid, first practiced by Ravaut, was later modified by Marinesco, Ogilvie, Fordyce and others, who have added solutions of arsphenamin to the plain serum or to the arsphenamized serum of the patient. Kolmer[7] has made further modifications which consist essentially in saturating the patient with mercury or potassium iodid before giving the intravenous injections, and in drawing the blood into sodium citrate solution immediately after the intravenous injection. The solution of arsphenamin (usually 0.0003 gm.) is then added to 10 c.c of serum and heated for thirty minutes at 56 C. About 30 c.c. of spinal fluid are drained off and the arsphenamized serum is injected. The principal advantages advanced by Kolmer for this technic are: (1) time saved, due to drawing the blood into citrate; (2) combining intravenous and intraspinous medication with mercury and potassium iodid, and (3) drawing 30 c.c. of fluid and injecting only 10 c.c., giving, thereby, the advantage of spinal drainage.

How much of the efficacy of the intraspinous medication depends on the irritation set up by the serum introduced, and how much depends on the direct action of the arsphenamin held in solution, remains to be determined. If the therapeutic action of the serum be due alone to the irritation induced, it may be argued that the addition of arsphenamin merely intensifies this irritation, and that the better results obtained from arsphenamized serum are due to the increase in the irritative quality of the serum and not to the spirocheticidal action of the arsphenamin.

Swift[8] has shown that blood drawn one hour after the injection of a full dose of arsphenamin contains approximately 0.000016 gm. of arsphenamin per cubic centimeter. Thirty-five cubic centimeters of serum, which have been drawn about fifteen minutes after the intravenous injection, would, therefore, contain at least 0.00056 gm. of arsphenamin, if not more. Kolmer[7] has added, as a rule, only 0.0003 gm. (with a maximum of only 0.0009 gm.) in 10 c.c. of serum, which would give, therefore, a dosage of only 0.00046 gm., as against 0.00056 gm. by the older method. Fordyce[9] adds, as a rule, 0.0005 gm. of arsphenamin to 10 c.c., which would be equivalent to 30 c.c. of serum, and instead of spinal drainage, as practiced by Kolmer, he mixes the serum thoroughly with spinal fluid before reinjecting, for the purpose of bringing about greater diffusion in the spinal fluid.

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[6] Hall, A. W., in discussion on Bassoe, Peter: Swift-Ellis Intraspinous Injections for General Paresis, Arch. Neurol & Psychiat. **2**:485 (Oct.) 1919.

[7] Kolmer, John A.: A Method of Treatment for Neurosyphilis, J. A. M. A. **74**:794 (March 20) 1920.

[8] Swift, Homer F.: Intraspinal Therapy in Syphilis of the Central Nervous System, J. A. M. A. **65**:209 (July 17) 1915.

The minute quantities of arsphenamin injected, even when the serum has been "fortified," are insignificant as compared with the amount of arsphenamin required to be of any therapeutic value when given intravenously. At Rush Medical Dispensary, Dr. Bertha Shafer found that 0.1 gm. of arsphenamin injected intravenously daily for long periods did not impede the progress of the secondary manifestations of syphilis. Therefore, it would seem to be illogical to expect sufficient spirocheticidal activity from the minute amounts contained in, or added to, serum which is injected intraspinously every two to four weeks, to be of much value therapeutically.

Dercum[2] is emphatic in his statements concerning the futility of intraspinal injections. He says the method is unscientific, because it is based on the mistaken view that the nutrition of the nervous system is carried on by means of the cerebrospinal fluid. Dercum points out that substances introduced into the cerebrospinal fluid rapidly disappear, passing through the arachnoidal villi into the venous system without entering the parenchyma of the central nervous system. The only action that can be ascribed to arsphenamin introduced into the subarachnoid space in simple solution is the inflammatory process set up by the drug. Dercum made use of the Swift-Ellis method of treatment in a large series of cases, but abandoned it entirely in favor of spinal drainage, on which, in his opinion, the efficacy of the older method depends.

DERCUM'S TECHNIC OF SPINAL DRAINAGE

With the method of spinal drainage, as carried out by Dercum, the patients are put to bed and every possible drop of spinal fluid is withdrawn at weekly or biweekly intervals. The improvement that takes place after this procedure is much more striking, according to Dercum, than that which follows the introduction of arsphenamized serum. The drainage results in a fall in the intradural pressure, which theoretically should be followed by an increased vascularity in the cord, similar to

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[9] Fordyce, J. A.: Intraspinal Therapy in Neurosyphilis, Am. J. Syphilis **3**:337 (July) 1919.

Bier's hyperemia. The spinal fluid drawn off is rapidly replaced, and thereby lavage occurs. The increase in the pressure of the spinal fluid in tabes and paresis is due, as a rule, to obstruction in the arachnoidal villi, and in the lymphatics to the outflow of the fluid. The spinal drainage, therefore, is a successful method of overcoming the increase in pressure of the fluid and the consequent reduction of vascularity of the brain and spinal cord.

AUTHOR'S TECHNIC

In a series of cases forming the material on which this report is based, slightly modified Swift-Ellis technic was followed. At first the exact method described by Swift and Ellis was used. Later slight modifications were made from time to time in an effort to determine the tolerance of the patient for increased doses of the serum, and to lessen as much as possible the reactions following intraspinal injections. In some cases an amount of spinal fluid approximately twice that of the amount of serum injected was withdrawn. Some of these patients, however, developed a severe headache after leaving the hospital. This practice was, therefore, discontinued, and later, as a rule, we withdrew slightly less fluid than the amount of serum injected. If an insufficient amount of fluid was withdrawn, the root pains following the injections seemed to be intensified.

The technic of the injection as used during the period between January, 1914, and October, 1918, was as follows: In the early afternoon the patient was given an intravenous injection of arsphenamin. From fifteen to forty minutes after the injection, about 100 c.c. of blood were withdrawn into a sterile bottle of that capacity. The bottle was stoppered and allowed to stand at room temperature until clotting had taken place. It was then placed in the icebox where it was kept over night. The following day the serum was decanted, centrifugated and inactivated in the usual manner. About 35 c.c. of this serum, undiluted with either salt solution or spinal fluid, were injected into the spinal canal after withdrawing approximately an equal quantity of spinal fluid. As a rule, one or two hypodermic injections of morphin were necessary during the night to control the pain. Many patients, however, did not complain of pain, and practically all of them left the hospital by noon the following day. The spinal fluid was then examined and the four principal tests, namely, the cell count, the globulin reaction, the Wassermann reaction using 0.2, 0.4, 0.6, 0.8 and 1 c.c., and the Lange gold chlorid reaction, were made after each injection. In this way we had a careful serologic control showing the progress of the therapy.

During this five year period we did not "fortify" the serum, after the manner of Fordyce and Ogilvie, by the addition of a solution of arsphenamin. Some of the early reports of the injections of arsphenamin and neo-arsphenamin directly into the spinal canal mentioned the loss of sphincter control in an occasional case, and we preferred to err on the side of conservatism rather than to take chances of possible damage to the patient. Recently, however, we have been using the method described by Fordyce, and at a later date we shall be in a position to make a comparison of the results of the two methods.

All of our patients who were treated by means of the intraspinal injection were given a series of intravenous injections before beginning the intraspinal treatment, and only those patients who did not respond to the intravenous medication were treated intraspinously. No one who has given intraspinal injections to patients who have not responded to intravenous injections can fail to see the great value of the subdural injection. Whether this be due to irritation of the serum, to the spirocheticidal action of the arsphenamin contained therein, or to the spinal drainage which incidentally takes place, the fact remains that the Swift-Ellis method will bring about marked serologic and clinical improvement in cases that have failed to respond to intravenous medication alone. This is particularly true in those patients with a high cell count and strongly positive fluid. One patient seen at Rush Medical College who had an intense headache and a partial hemiplegia, which had persisted in spite of eight intravenous injections at frequent intervals, was given one intraspinal injection in the usual way. The fluid showed 1,000 cells and the other findings were likewise strongly positive. After this one injection the pain promptly ceased and the partial hemiplegia cleared up.

CASES STUDIED

The clinical material forming the subject of this review consists of fifty-two private patients with syphilis of the central nervous system, treated during a period of approximately five years between January, 1914, and October, 1918. Patients coming under treatment since October, 1918, are not included in this series, because insufficient time has elapsed since beginning the treatment to justify a conclusion concerning the ultimate result.

Of the fifty-two cases there were twenty cases of paresis, twenty-five cases of tabes dorsalis, and seven cases of central nervous system syphilis, such as meningitis and arteritis. The fifty-two patients received three hundred and ten intraspinal injections which, as a rule, were given at monthly intervals. For obvious reasons, it was impossible to control the patients in all cases. Some paretic patients were so unruly when first coming under observation, and such a burden to their families, that it was thought better to have them committed to institutions rather than attempt to attain an improvement, which at best could be only temporary. Some of these patients died of intercurrent infections and one committed suicide. A few of the patients lived in distant cities and the time and money necessary for travel made the injections almost prohibitive. Therefore, a statistical study of the group does not do justice to the value of this method of treatment as a detailed report of the individual cases would do, but nevertheless, the statistical study is of value in aiding us to arrive at a prognosis in future cases.

Of the twenty patients with paresis, eleven are now dead. It is an interesting fact that these eleven patients received an average of 3.5 injections each, whereas seven paretics who are much improved clinically and are still living received an average of fifteen injections each. Therefore, it is fair to assume that had it not been impossible, for reasons mentioned above, to give these patients more injections, some of them at least might still be living. Two paretics, who are still alive, show thus far little improvement either clinically or serologically.

Of the twenty-five patients with tabes, thirteen show marked clinical improvement, and at the last examination the spinal fluid was negative. Ten patients are much improved clinically, but the fluid is still positive. Two of the patients with tabes have passed from our control, and their present condition is unknown.

Of the seven patients with central nervous system syphilis other than tabes or paresis, four patients are much improved clinically and have negative spinal fluids. In one case the fluid cleared and later became positive. In another case the fluid remains strongly positive.

CONCLUSIONS

1. The Swift-Ellis intraspinal method of treatment of syphilis of the central nervous system is superior to intensive intravenous treatment alone.

2. Whether the efficacy of the method of treatment depends on (*a*) the irritative action of the serum, thereby increasing the permeability of the choroid plexus for arsphenamin; on (*b*) the spirocheticidal action of the arsphenamized serum, or on (*c*) spinal drainage, remains to be determined.

3. The method is perfectly safe when care is exercised in technic and in the proper selection of cases, and should be resorted to in all cases in which the patient fails to respond to intravenous medication.

25 East Washington Street.

TWO CASES ILLUSTRATING UNUSUAL MANIFESTATIONS OF SYPHILIS *

1. GUMMA OF THE BLADDER
2. URTICARIAL SYPHILID

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REPORT OF CASES

CASE 1.—The salient features of the case are: A gummatous invasion of the bladder wall resulting in dysuria, leading to an erroneous diagnosis of gonorrhea; cystoscopic examination revealing a sharply marginated growth in the bladder wall; a positive Wassermann reaction, and prompt relief after institution of anti-specific treatment.

History.—A woman, aged 21, first seen Sept. 10, 1919, was referred to me by Dr. J. J. Eklund. She appeared to be well nourished, was 5 feet, 2 inches tall and weighed about 130 pounds. She admitted having had gonorrhea some time previously, but denied any other infectious disease and had always been well.

Her chief complaint was frequent and painful urination which had lasted for four months, continually growing worse. She had been treated for a supposedly gonorrheal cystitis with bladder irrigations and internal medication, but without benefit. The urination was more frequent at night; there was a constant feeling of discomfort in the bladder region, and a radiating pain toward the left groin.

Urinary and Bladder Examination.—The urine showed abundant pus cells and a few red blood cells intermingled. Gonococci could not be demonstrated, but there were other unidentified bacteria. Cystoscopic examination showed that the bladder was especially inflamed in the region of the trigone. Both ureters seemed to be functioning normally. A growth about 2 cm., back of the left ureteral orifice could be distinctly seen. This measured about 2.5 cm. in diameter, was raised about 0.5 cm. from the normal bladder surface, was sharply marginated and quite round; it had certain bleeding points near its center. Thus it had the appearance of a nonpedunculated, mildly inflammatory papilloma.

General Examination.—There was positively no evidence of old or recent skin lesions. There were, however, small, hard and easily palpable glands in the groin, more particularly on the left side. There was a slight vaginal discharge; smears were negative to gonococci. There was no particular cervical irritation or vaginal inflammation. She did not look anemic; the hemoglobin was 90 per cent. and there were 4,800,000 red blood cells. The blood Wassermann test was + + + +.

Treatment.—Specific treatment was started on September 11. This was followed by definite and prompt improvement, the urinary symptoms becoming less disturbing immediately. By October 1 there was great relief. A cystoscopy done on October 5 showed that the tumor had entirely disappeared and that only a slight inflammatory area could be seen where it had been previously. She has kept up treatment faithfully, and is now apparently well.

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* From the Dermatological Department, the Duluth Clinic.

COMMENT

There appears to be no reason to doubt that this was a case of gumma of the bladder.

Lloyd Thompson[1] has reported eighty-four cases in the literature. Of these eighty-four cases, he thought fifty-eight were authentic. In 1901, MacGowan[2] reported a gumma of the bladder diagnosed by cystoscopy. Haberdeen,[3] in 1911, reported the first case in which a Wassermann test confirmed the diagnosis.

Case 2.—This case presented severe, urticaria-like lesions which rapidly appeared and disappeared, producing raw surfaces and gradual pigmentation.

History.—The patient was a man, aged 26, a painter. He was seen first Dec. 1, 1919. He acknowledged a few of the exanthemata, but had never been seriously sick. After returning from the A. E. F. he developed a skin rash accompanied by severe itching. It gradually spread despite various forms of treatment, and covered a large part of his body.

General Examination.—The patient looked pale, tired and worried. His height was 5 feet, 10 inches and his normal weight was 175 pounds, but he had lost 25 pounds since the beginning of his illness.

He had had a little hoarseness for some time, but a nose and throat specialist whom he had consulted could find nothing wrong with his throat. Hard, shotlike glands could easily be felt in the groin, and a few in the posterior occipital region. The epitrochlears could not be felt. The urine was negative; blood pressure was normal; hemoglobin, 70 per cent.; red blood cells 3,500,000, and white blood cells 9,000.

Description of Skin Lesions.—The whole skin was plastered with ointment of zinc oxid, for the time being rather fully concealing the character of the skin lesion. On Dec. 5, 1919, the rash had become very troublesome, and he was unable to put on his clothes. Over the back, chest, neck and arms, as well as on his legs, were patches varying in size from 1 to 7 or 8 inches in diameter, in places raised ⅛ inch over the normal surface, and sharply marginated. In the center of most of the patches there were thin scales. Raw spots developed, particularly at points of rubbing or irritation—in the region of the buttocks and neck especially. The itching and burning were severe. Besides these large lesions, there were a few smaller squamous lesions here and there, and some discoid patches on the forehead. It was noted that some of the urticaria-like lesions, and even the large raw places, disappeared in twenty-four hours, and new ones elsewhere reappeared. Pigmentation was prone to develop early in those that showed healing.

Course and Treatment.—Ten days after the first intravenous injection of arsphenamin the itching had greatly abated, and in two weeks no urticarial lesions or raw spots could be seen. The squamous lesions were a little slow in disappearing, and considerable pigmentation continued to develop. The hoarseness was still slower in disappearing. He gained in weight rapidly. At the present time (March 28, 1920) he is in excellent condition.

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[1] Thompson, Lloyd: Syphilis of the Bladder, Am. J. Syphilis **4**:50 (Jan.) 1920.

[2] MacGowan: Cutan. & G.-U. Jour. of New York, 1901.

[3] Habereen, J. P.: Zentralbl. f. chir. **38**:663, 1911.

COMMENT

This case is reported because of the rare, urticaria-like skin lesions and the extensive raw areas, which are equally rare in syphilitic patients.

OBSERVATIONS ON THE TREATMENT OF SYPHILIS

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Syphilis generally is probably as poorly treated as any disease with which we have to contend. Every medical man properly includes syphilis in his field, and should know the modern methods of treatment; unfortunately, many do not. A survey of specific therapy administered to approximately 3,000 civilian syphilitic persons by reputable physicians reveals some rather startling facts. In September, 1919, I[1] reported as follows: Of 113,000 men examined at Camp Travis, 3,000 were found to have infectious lesions of syphilis. A fair proportion of these had consulted reputable physicians at one time or another, and yet we gleaned such facts as the following from their histories: Local caustic and antiseptic applications were freely used by physicians and patients alike, not a single dark field examination having been made in any case prior to entering the service. A negative Wassermann reaction during the first few days of the infection was accepted as sufficient evidence of the absence of syphilis. Late syphilis with negative Wassermann reactions were usually missed. Treatment with pills and mixed treatment were the usual methods employed, but five men having received the equivalent of a single eight-week course of treatment such as outlined by the Surgeon-General's committee on venereal diseases. There seemed to be no plan of treatment other than that directed by the visible manifestations of the disease, and when these disappeared, treatment stopped. The reason why the average doctor believes deep down in his heart that syphilis is an incurable disease is readily understood when his treatment of the disease stands in the light of our present knowledge.

It should be considered criminal deliberately to await the appearance of secondary manifestations of the disease before starting treatment. The so-called tonic treatment should be relegated to antiquity because we now recognize that we are dealing with a constitutional infection that is caused by a specific organism that may be destroyed in vivo as well as in vitro by definite spirocheticides which in sufficient concentration will destroy every organism encountered. If we were able to stop there, the immediate cure of syphilitic persons would indeed be a simple matter, but unfortunately there are further considerations. We know that the spirochete has a certain affinity for epithelial structures, that it attacks all tissues and organs, and that further, as demonstrated by Nichols,[2] different strains may determine selective localization of spirochetes difficult to reach with our drugs. Warthin [3] describes in minutiae the pathology of syphilis, and states that he has never seen pathologically a cured case of syphilis, but neglects to tell us what treatment cases had had that came to his necropsy table. He shows the facility with which the spirochete localizes in different tissues and perhaps underestimates our ability to destroy the organism. We are limited in our therapeutic attack by the ability of our patients to tolerate drugs, and while toleration varies considerably in different persons, there are certain limits beyond which we dare not go. We estimate dosage of arsphenamin according to the body weight of the person, usually at the rate of 0.1 gm. to each 30 pounds of body weight, because this is well above the amount that is effective from a therapeutic standpoint, and at the same time clinical experience has shown that such an amount may be given with comparative safety. In using mercury we are limited to dosage that will not salivate our patients or damage vital structures, regardless of the salt used or the method of introducing it into the body, and yet we are able to accomplish much with mercury either alone or used in conjunction with arsphenamin.

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[1] Guy: Analysis of the Venereal Situation, Urol. & Cutan. Rev. **23**:512 (Sept.) 1919.

ARSPHENAMIN AND MERCURY MEDICATION

The relative efficiency of the drugs is in the minds of many an open question. Kolmer's [4] work in vitro-vivo with arsphenamin and mercury in experimental trypanosomiasis demonstrated trypanocidal action for arsphenamin in a dilution of 1 : 40,000, and at the same time conclusively demonstrated the superiority of arsphenamin over mercury as a trypanocide. Although we repeatedly examined primary lesions after the injection of a full therapeutic dose of arsphenamin, we were unable to find spirochetes later than one hour and a half after the treatment. When examinations were made at ten minute intervals actively motile spirochetes were first noted, then those with feeble motility, then nonmotile and distorted forms, and finally the absence of organisms. On the other hand, I have on several occasions noted spirochetes seventy-two hours after an injection of mercury. And yet Ehrlich failed in his attempted "therapia magna sterilisans." The principle reason for his failure was the rapid elimination of the drug. Swift and Ellis [5] were able to find no spirocheticidal activity of blood serum six hours after the injection of a full therapeutic dose of arsphenamin. Another reason for Ehrlich's failure is the facility with which the spirochete buries itself far from the general circulation.

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[2] Nichols, H. G.: Observations on a Strain of Spirochaeta Pallida Isolated from the Nervous System, J. Exper. M. **19**:362, 1914.

[3] Warthin, A. S.: The New Pathology of Syphilis, Am. J. Syphilis, **2**:425 (July) 1918.

[4] Kolmer: Chemotherapy of Trypanosomiasis, J. Infect. Dis. **20**:10, 35 (Jan.) 1917.

[5] Swift and Ellis: New York M. J. **96**:53, 1912.

In order to overcome these difficulties Pollitzer[6] states that "salvarsan should be administered in sufficient dosage, repeated at such intervals that the blood is kept charged with the drug for several days continuously." He approaches these conditions by giving arsphenamin on each of three successive days at the rate of 0.1 gm. to each 30 pounds of body weight, followed by a course of mercury. By this method he has been able to bring about a reversal of the Wassermann reaction in cases in which it has been persistently positive after repeated courses of less intensive medication. He also reports a series of patients with primary syphilis—in which the diagnosis was made by the dark field method, the Wassermann reaction being negative—in which a single such course was given. After about a year there was no indication either clinical or serologic of syphilitic infection. I have treated twenty-five patients in a similar condition in the same manner, and have kept ten of them under observation for a year without being able to demonstrate clinical or serologic evidence of remaining infection. In ten other patients with primary syphilis, three of whom already had positive Wassermann reactions, I have used a modification of his plan. As soon as the diagnosis was established, arsphenamin at the rate of 0.1 gm. to each 30 pounds of body weight was given on each of three successive days; two weeks later this treatment was repeated; and in a month three more injections were given, making a total of nine injections in six weeks. With this, weekly injections of the mercuric salicylate were given for a total of ten weeks, making a total of nine injections of arsphenamin and ten of mercury in ten weeks. Six of these patients were under observation for a year with negative results; the other patients were lost by transfer to other camps or overseas. The balance of our primary cases, numbering about 365, were given routine treatment according to the plan of the Surgeon-General's advisory committee. These patients were given two complete courses, each comprising eight injections of arsphenamin and eight of mercury, the therapeutic rest period being five weeks. We have been unable to keep many under observation for a year, but the majority of them were clinically and serologically negative when last examined. About a third of the patients were under observation for at least eight months. One developed an annular macular eruption and four others were found to have positive Wassermann reactions within this time. In young, robust persons with primary lesions our aim is to abort the disease by destroying every infecting spirochete, and this may be done with a reasonable degree of certainty when we overcome the obstacles to Ehrlich's hoped for immediate therapeutic victory.

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[6] Pollitzer, S.: The Principles of the Treatment of Syphilis, J. Cutan. Dis **24**:633 (Sept.) 1916.

LENGTH OF TREATMENT AND DOSAGE

There are two ways in which we may expect to destroy more spirochetes in a given length of time; one is by giving arsphenamin at more frequent intervals, and the other is by increasing the amount administered at each injection. I have repeatedly given arsphenamin at the rate of 0.1 gm. to 20 pounds of body weight, up to and including 0.8 gm., without reaction. In one patient weighing 120 pounds, 0.5 gm. was given on each of three successive days without untoward results. With manufacturers offering a drug of much lower toxicity than formerly it seems logical to take advantage of the opportunity to increase our therapeutic results. A plan to keep the blood stream saturated with arsenic for a considerable number of hours that is worthy of mention is that of Reiger.[7] He uses neo-arsphenamin, on account of the low toxicity, giving 0.9 gm. at the first injection, 0.6 gm. in an hour and 0.3 gm. at the end of the third hour. The time and amount of the injections are based on the elimination rate of the drug. Much better clinical results are claimed by this than by ordinary methods. The theory is advanced that arsenic will reach the spinal fluid in appreciable amounts after such treatment.

Fordyce[8] believes that in routine work, injections should not be given at shorter intervals than from five days to a week, and in this respect most syphilographers are in accord, favoring rather a method of fractional sterilization than to attempt an immediate therapeutic victory. Short, intensive courses of arsphenamin and mercury used in conjunction are favored. Such methods have the advantage of comparative safety over more intensive treatment, and certainly no one can discount the results that have been obtained. The length of courses varies in different hands, but usually comprises from eight to ten weekly injections of arsphenamin and the same number of injections of mercury, followed by a period during which no medication is given. The necessity of rest periods during antisyphilitic treatment was long ago pointed out by Fournier. In the laboratory, Noguchi[9] has been able to increase the tolerance of spirochetes for arsphenamin five to six fold by gradually increasing the amount of the drug in his culture medium. The toleration for mercury was increased from thirty-five to seventy times the original. He also found that this acquired immunity on the part of the spirochete to the action of arsphenamin and mercury would disappear on cultivation in mediums free of the drug. Thus Noguchi produced scientific proof of the accuracy of Fournier's clinical observations and placed on a scientific basis the prolonged intermittent treatment of syphilis. The patient should be given a rest period of sufficient length to recover physically from the course of treatment just finished, as well as to prevent the formation of an arsenic and mercury fast strain of spirochete from too sustained treatment, the time being limited by the probable date of clinical or serological recurrence. I consider that a period varying from five to eight weeks is required. At the close of a rest period a Wassermann reaction will be obtained that will give a more reliable check on the results of therapy than that which might be taken while the patient is on active medication.

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[7] Rieger, J. B., and Solomon, H. C.: The Circulation of Arsenic in the Cerebrospinal Fluid, J. A. M. A. **71**:15 (July) 1918.

[8] Fordyce, J. A.: Diagnosis and Treatment of Syphilis, Am. J. Med. Sc. **152**:469 (Oct.) 1916.

[9] Akatsu Seinai and Noguchi Hideyo: The Drug Fastness of Spirochetes to Arsenic Mercurial and Iodide Compounds in Vitro, J. Exper. Med. **25**:349 (March) 1917.

DEPENDENCE OF TREATMENT ON INDIVIDUAL AND ON STAGE OF DISEASE

Regardless of theories and plans for the treatment of syphilis, however, we must remember that we are treating a patient as well as a disease, and govern ourselves accordingly. Absolute generalization in the application of specific therapy will lead to disaster. All patients may not be treated intensively. Some will not tolerate mercury in one form or another, and there are some who cannot tolerate arsenic. One must be very cautious in the application of antisyphilitic treatment, particularly with pathologic conditions affecting the cardiovascular, renal and pulmonary apparatus, and with modifications of therapy as the result of such pathology, one must necessarily continue treatment much longer. Again, the kind and amount of treatment will vary with the stage and location of the disease. One is justified in disregarding the possibility of reaction following arsphenamin in order that treatment may be started twenty-four hours sooner in cases of dark field positive cases than would otherwise be possible. It is obvious that a patient with a primary lesion will require less treatment than one with florid manifestations of an early generalized infection; he, in turn, will require less treatment than a patient with a long standing infection, and the patient with evident infection of the central nervous system will require more treatment, and in many cases the application of special therapy, to reach the disease. The chances of a cure are to some extent dependent on not only the kind of treatment that the patient receives, but also on the status of the infection at the time treatment is instituted. Our ideas as to the amount of treatment necessary to cure syphilis are largely empiric, but we no longer blindly state that from three to five years of mercurial treatment are necessary to cure any case of syphilis. The advent of arsphenamin has materially shortened the time, as has also early diagnosis by the dark field method and correspondingly early institution of vigorous specific treatment. In the Wassermann reaction we have an invaluable aid in determining the effect of therapy, but in order that we may arrive at any definite conclusions bearing on the question, we must take into consideration the opinions of close observers with vast experience in modern therapy. Fordyce[8] states that in primary syphilis, before the Wassermann reaction has become positive, it is possible to abort the infection; that such patients should receive two courses of arsphenamin and mercury used in conjunction; that in secondary syphilis three courses is usually the minimum required; while in tertiary cases the method of treatment depends on the tissues or organs involved. Using weekly injections of arsphenamin and an insoluble salt of mercury in six-, eight- and ten-week courses, we consider that one course will cure a certain percentage of cases, but that two courses are usually needed. Pollitzer shows that one course such as he advocates will cure, but gives his patients an additional course of the same kind "for insurance." Of patients with secondary manifestations at the time of the beginning treatment, I require a negative Wassermann reaction and negative clinical findings after each of three consecutive courses of treatment. This has often meant four, five or six courses instead of three, but I believe it is necessary, because when the patient becomes asymptomatic, our principal guide is the Wassermann reaction, and failure to cause its reversal after a course, or a return to positive after the reaction has been negative spells an active infection.

Of about 2,500 patients with early or secondary syphilis, comparatively few were held in camp sufficiently long to complete three courses of treatment; many of them were sent to France after a single course of treatment if the Wassermann reaction was negative, and they were free from lesions, treatment being continued on their syphilitic registers regardless of where they were sent. It is interesting to note that eight weekly arsphenamin and a similar number of mercury injections caused a reversal of the Wassermann reaction in over 98 per cent. of these cases. Approximately 1,000 men received two courses and about 300 were given three courses, a few patients with refractory cases receiving additional courses according to the indications. None of these patients had been under observation sufficiently long to justify any conclusions regarding the end results of the therapy. As a rule, the older the infection the most difficult it is to cure. In late cases, repeated courses plus the iodids, for their effects as resolvents of specific infiltrations, are necessary. When we have given the treatment we believe to be indicated, and have obtained repeated negative Wassermann reactions in addition to a clinical cure, we stop all treatment, keeping the patients under observation for at least a year during which the Wassermann tests are made every two or three months. With negative clinical and serologic findings at the close of the year of observation, it is customary to give a provocative injection of arsphenamin and to repeat the Wassermann test. As to the value of the provocative treatment, physicians do not agree. We know that the antibody content of the syphilitic blood may vary from time to time to such an extent that at one time the reaction may be weakly positive and the next time frankly negative. In an attempt to obtain some information on the subject we have in some cases used the provocative injection and in others merely repeated the Wassermann test at intervals. The number of cases available for this comparison was unfortunately too small to be conclusive, but we were not able to demonstrate provocative properties for small injections of arsphenamin. It is our impression that two- or three-week courses of iodids at times produce positive Wassermann reactions in clinical syphilis with negative tests. We have no definite data to offer in support of this theory; it is a clinical impression only, as far as we are concerned. We have used the method many times and apparently in a fair percentage of our few cases with provocative results, but the same objection holds in these cases that does in the case of the provocative injection of arsphenamin.

INTRASPINAL THERAPY

Before any patient with syphilis is finally discharged a lumbar puncture is made to determine the presence or absence of infection in the central nervous system. If there is any indication of neurologic involvement before this time, of course, we do not wait, but when we realize that most of our central nervous system infections are cured by the treatment usually applied, as evidenced by the discrepancy between the number of cases showing early positive spinal findings and the infrequency of positive findings after ordinary treatment, certainly routine treatment should be given a thorough trial before special therapy is resorted to. A small group of patients with infections not more than six months old were punctured in my service and positive findings noted in 10 per cent., as evidenced by a cell count of over five, an increased globulin and a positive Wassermann test or certain changes in Lang's gold test. These patients were put on routine treatment and after two complete courses were again punctured, and only one case was doubtfully positive. It is interesting also to note that one-half of the cases with persistently positive Wassermann reactions after two courses of treatment had positive spinal fluid findings. Fordyce[8] reports positive spinal findings in 20 per cent. of one series of secondary syphilis and 25 per cent. in another, and says it is his belief that the spirochetes are destroyed spontaneously or by therapeutic agents administered in the usual way. Obviously, early intensive treatment will prevent most late neurologic complications. The older the infection the greater the likelihood of such involvement and the more difficult its eradication.

In patients with persistent inflammatory changes in the spinal fluid additional intensive intravenous medication may bring about the desired result, or intraspinal therapy, or a combination of the two may have to be used. The same general principles hold in the sterilization of a focus of infection in the central nervous system as in the general treatment of the disease, but a modified method of therapeutic attack is necessary on account of the anatomy of the part. Direct saturation of the spinal fluid with comparatively large amounts of arsphenamin or mercury is impracticable on account of the irritating effect, and in some cases fatalities, due to overdosage. The original technic of Swift and Ellis [10] or the modification of Ogilvie,[11] with the direct addition of arsphenamin to blood serum, are the methods most in vogue at the present time. Dosage is begun with minimum amounts and gradually increased if well tolerated, about 0.5 mg. being considered the limit of safety. Treatments are given in courses, the intervals between them varying according to the reaction after each injection. Much has been said from a theoretical standpoint against intraspinal therapy, but no amount of scientific discussion can discount results that have been obtained when the method has been properly used. Speaking from a prognostic standpoint, Fordyce [12] says: "When symptoms are due to an active inflammation with strongly positive fluid, the outlook is very encouraging. Where, however, the underlying process is one of degeneration with atrophy and sclerosis, with negative or weakly positive fluid findings, the prognosis is not so hopeful."

There are those who condemn the method unreservedly, and there are those who are accused of being overenthusiastic, and according to their faith, the indications vary in the minds of different men. I should be inclined to exhaust intensive general medication before resorting to intraspinal therapy, and having done so, I should expect some clinical results in cases in which the pathologic process was not too far advanced.

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10. Swift, H. F., and Ellis, A. W. M.: The Treatment of Syphilitic Affections of the Central Nervous System with Especial Reference to the Use of Intraspinous Injections, Arch. Int. Med. **12**:331 (Sept.) 1913.

11. Ogilvie: J. A. M. A., 1914, No. 63.

12. Fordyce, J. A.: Syphilis of the Nervous System, J. Cutan. Dis. **34**: 713 (Oct.) 1916.

ACIDOSIS IN SKIN DISEASES *

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MINNEAPOLIS

Our attention was first called to the subject of lowered alkalinity in seborrheic eruptions by the article of Barber and Semon [1] published in 1918. In a series of observations on soldiers in the British army, who had seborrheic eruptions, they found a pronounced and remarkably constant hyperacidity of the urine. This led them to the assumption that the seborrheic state is really a manifestation of relative acidosis. When the possibility of the existence of acidosis occurred to them, they began to test the therapeutic effects of giving alkali mixtures and making local applications of alkalies. Beneficial results were immediately apparent. From their clinical and chemical (urine) examinations, they considered that they had established these two fundamental facts:

1. That the majority of patients with seborrheic manifestations show a markedly increased alkaline tolerance, many of them to an astounding degree.

2. That in nearly all cases all active inflammatory processes cease, and the eruption rapidly clears when the urine has been rendered alkaline. Barber and Semon [1] did not examine the blood of their patients to determine whether there was a lowering of the alkali reserve, their investigations being limited to chemical examinations of the urine. In 1919, Schwartz, Levin and Mahnken [2] reported the results of examinations of the blood to determine the alkali reserve in 139 cases of various skin diseases. They found that 59.7 per cent. gave normal values, 35.9 per cent. showed a mild acidosis, while 3.5 per cent. gave a moderate acidosis, and one case had a severe acidosis, but the skin condition here was a complication of diabetes. Their

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

[1] Barber and Semon: Etiology and Treatment of Seborrhoeic Eruptions, Brit. M. J. **2**:245 (Sept.) 1918.

[2] Schwartz, Levin and Mahnken: The Alkali Reserve in Various Diseases of the Skin, J. Cutan. Dis. **38**:9 (Sept.) 1919.

conclusions were that a lowering of the alkali reserve has been found sufficiently often in acne, psoriasis, urticaria, furunculosis and eczema (especially seborrheic) to warrant further investigation.

In the series of cases which we have studied, we have selected only extensive and well-marked examples of the condition. We thought that if relative acidosis were a constant accompaniment, it should be more marked in extensive and widely spread cases.

In conversing with Prof. L. G. Rowntree, whose experience in acidosis studies is extensive, he stated that he had not encountered any particular integumentary manifestation, and we, therefore, conclude that if the "seborrheic state" were a manifestation of acidosis, it should be encountered with relative frequency by one who sees acidosis constantly and in a large number of cases, occurring in a variety of conditions.[3]

Acidosis is a condition in which the concentration of bicarbonates in the blood is reduced below the normal level.[4] It is a secondary occurrence in diabetes, nephritis, certain types of diarrhea, recurrent vomiting, food intoxication and in cases in which the patient is moribund. In our series of cases, we determined the alkali reserve and in cases in which there was a marked variation, or because of some special indication, we did a complete metabolic study, including basal metabolism, and thorough physical examination by an internist. This was done to rule out some other condition which might account for the acidosis present.

DETERMINATION OF ALKALI RESERVE

In determining the alkali reserve, we found the most dependable test was the Van Slyke.[5] Oxalated blood plasma was saturated with carbon dioxid by means of repeated rotation in a separating funnel with expired air. One cubic centimeter of this plasma was placed in the receiving cup of the Van Slyke apparatus and rendered alkaline with a drop of normal ammonia. One drop of 1 per cent. solution of phenolphthalein was used as an indicator. The mixture was covered with a few drops of ethyl alcohol and drawn into the apparatus by lowering the mercury bulb. The receiving cup was washed with from 0.5 to 1 c.c. of distilled water, and this washing was likewise drawn into the apparatus. Normal sulphuric acid was then placed in the receiving cup and permitted to flow into the apparatus until the total volume of 2.5 c.c. was reached.

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[3] Rowntree, L. G.: Personal communication.

[4] Sellard, A. J.: Principles of Acidosis, Cambridge, Harvard Press, 1917.

[5] Gradwohl, M.: Blood and Urine Chemistry, St. Louis, The C. V. Mosby Co., 1917.

The mercury bulb was lowered after closing the apparatus. The carbon dioxid found as sodium bicarbonate was liberated in a vacuum by the action of the sulphuric acid and the amount of carbon dioxid read off directly by leveling the mercury in the bulb, and in the graduated tube of the Van Slyke instrument. In all cases, the greatest care was taken to insure that the apparatus was absolutely tight, and to prevent the loss of carbon dioxid.

Normal values measured as tension of carbon dioxid are considered as varying from 80 to 53 volumes per cent. Figures between 53 and 40 volumes per cent. are taken to indicate a mild acidosis; figures below 40 volumes per cent. as more severe types of acidosis.

Alveolar air collections were made by the Ploesch method. The determinations were made on a Haldane instrument for air analysis, and the results given as tension in millimeters of mercury. The values found are essentially the same as those determined by the Van Slyke instrument, the source of the carbon dioxid being the same substance — sodium bicarbonate — in each case. Collection required the cooperation of the patient, however, and in many cases this was rendered difficult, or impossible, due to the patient's failure to understand the directions given. We used this method in some cases, but always depended on the Van Slyke instrument.

DETERMINATION OF BASAL METABOLISM

Basal metabolisms were determined after the patient had fasted fourteen hours. Air was collected in a spirometer, fashioned after the "Tissot" instrument. In each case, the patient breathed into the instrument for ten minutes, after being at absolute rest for half an hour. Duplicate air analyses were made in a Haldane instrument, and the total amount of oxygen absorbed calculated. The respiratory quotient being found, the calorific value of oxygen for the quotient in question was taken, and the number of calories of oxygen per square meter of body surface per hour calculated. Surface areas were derived from the du Bois tables and our normal figures from Miss Sandiford's table in use at the Mayo clinic. In some cases extensive eruptions on the face of the patient made the mask used in collecting the air very uncomfortable; this introduced an unavoidable element of error due to the restlessness of the patient.

Basal metabolism figures are given in percentages of deviation from the normal. Values less than 10 per cent. above or below represent normal metabolism.

SEBORRHEIC DERMATITIS

Barber and Semon[6] point out that the exudative diathesis of infancy is often a forerunner of what they call the seborrheic diathesis in adult life. In a urine and blood chemistry study of exudative cases, one does not find any degree of acidosis; in fact, the reverse is the tendency. There is an increase in fluids and there is no acetone in the urine. We were not able to find any literature on blood chemistry findings on patients with exudative diathesis. Inquiry among pediatricians disclosed the fact that in a large series of cases of acidosis observed, due to a variety of causes, no cases of infantile eczema or seborrheic dermatitis were encountered.[7]

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[6] Semon, H. C.: Sycosis Barbae. Practitioner **104:**48 (Jan.) 1920.

FINDINGS IN VARIOUS SKIN DISEASES

Name	80-53 Volumes per Cent. Normal	53-40 Volumes per Cent. Mild Acidosis	Remarks or Other Data
Seborrheic dermatitis:			
P. R.	65.3		
J. B.	61.4		
M. H.	61.4		
J. C. B.	....	52.5	Four months pregnant
M. H.	60.5		
H. B.	54.1		
M. P.	63.0		
Eczema:			
P. G.	65.4	....	Basal metabolism, 15 per cent.
J. T.	56.0		
D. O.	72.9		
Mrs. H.	60.5		
C. B.	....	44.3	Chronic interstitial nephritis; alveolar carbon dioxid, 3.95
C. M.	63.3		
W. O. F.	65.3		
A. G.	60.5		
M. J.	59.4		
T. L. D.	....	49.5	Beginning nephritis; focal infection; creatinin, 1.9; urea nitrogen, 30.0; uric acid, 4.1; hemoglobin, 71 per cent; blood sugar, 0.09
Psoriasis:			
A. C.	53.4		
L. C. C.	57.4		
W. E.	57.0		
G. G.	....	51.0	Nephritis; creatinin, 1.9; urea nitrogen, 25.6; uric acid, 3.42
H. W.	59.7		
H. W. W.	61.7		
Gar.	56.7		
Mrs. K.	....	49.5	Focal infection: arteriosclerosis; nitrogen retention
Parapsoriasis:			
P. L.	58.0		
Miss H.	57.0		
Acne vulgaris:			
J. L.	71.0		
E. J. O.	54.8		
T. B.	58.9		
G. L.	59.0		
G. K.	....	47.6	
A. M.	74.0		
Dermatitis herpetiformis:			
V. J.	67.0		
G. M.	58.6		
Acute lupus erythematosus (disseminated)			
A. W.	....	47.8	Moribund
Acute exfoliative dermatitis:			
M. M.	62.0		
Alopecia universalis:	60.4		
Furunculosis:			
G. H.	57.65		

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7. Seham, M.: Personal communication.

In our own studies, we have been unable to establish the existence of a seborrheic state, or seborrheic diathesis. We have found no consistent change in the alkali reserve and have not found even a mild acidosis which could not be accounted for.

The alkali therapy in our hands has not been successful. We have obtained better results by placing the patients on a fat-free diet and using the ordinary well-known lotions and ointments.

PSORIASIS

We thought that if any disease would show a metabolic change, psoriasis would. The psoriasis cases were selected. Only well-marked, widely distributed cases were chosen, and these were chosen at the height of an outburst. In no cases did we find a marked change in the alkali reserve. Complete blood chemistry was done in four cases, and in all four there was an increased urea nitrogen. In three cases of psoriasis there was marked focal infection. One patient with psoriasis had a marked arteriosclerosis, although he was only 22 years of age. Rest in bed and cleaning up of foci caused such remarkable improvement in his general condition that the psoriasis, which had previously been inveterate, promptly responded to treatment. From this small experience with psoriasis, we have decided that it is advisable to have every psoriatic patient carefully examined by a competent internist, especially for infected foci.

We used alkalies in the treatment of ten patients with psoriasis, giving heavy doses of sodium bicarbonate internally and paste of equal parts of sodium bicarbonate and petrolatum externally. In none did we find striking improvement. One patient became quite ill from the heavy bicarbonate dosage (2 ounces, three times a day). He complained of severe depression, anorexia and marked irritability.[8]

CONCLUSIONS

1. We could find no marked, nor consistent change in the alkali reserve in psoriasis, acne vulgaris, eczema and seborrheic dermatitis.

2. Promiscuous alkali therapy is unscientific and inadvisable, and may produce a condition of alkalinosis which may be dangerous to the patient.

REGARDING BLOOD OR URINE CHEMISTRY

3. We have failed to find in the blood and urine the evidence of the so-called "seborrheic state."

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[8] Bayliss, W. M.: Acidosis and Hydrogen-ion Concentration, Brit. M. J. **2**:395 (Oct.) 1918.

4. We depended on the Van Slyke test in acidosis. The advisability of accepting changes in urinary acidity as evidence of acidosis is questionable, especially when such a simple and accurate test as the Van Slyke is obtainable.

5. We realize the number of cases studied is not conclusive, but they are suggestive of negative findings.

625 Syndicate Building.

ABSTRACT OF DISCUSSION

Dr. Richard L. Sutton, Kansas City, Mo.: I have found alkaline therapy efficient in infantile eczema, furunculosis and infectious eczematoid dermatitis. It is important to emphasize one of the points made by the authors, and that is, to be sure that excessive amounts of alkalies are indicated and can be taken care of by the patient. Otherwise, one is liable to come to grief.

Dr. Augustus Ravogli, Cincinnati: The acidosis has a great deal of influence on the collagenous tissues. If we try to dissolve fibrin in some acid solutions the fibrin does not dissolve, but if we add some alkaline substance, then the fibrin will dissolve. The same thing happens in the collagenous tissues of the skin which, as a consequence of the acidosis, are made impermeable, and this causes edema. The edema is produced by the collagenous tissues retaining the serum, or better the lymph, as it is difficult for the albumin to be dissolved. The albumin in the urine when the kidney is inflamed is just the same condition as edema in the skin.

Dr. Samuel E. Sweitzer, Minneapolis: We were disappointed at not being able to find acidosis, because when I began this work I thought that if some of the cases of seborrheic dermatitis and of eczema were due to acidosis it would be of value. We were disappointed at not being able to come to agreement with other writers in regard to this matter.

Correspondence

"THE NEED FOR THE STUDY OF RINGWORM IN AMERICA"

To the Editor:—In the April issue of the ARCHIVES appeared an editorial signed with initials, in the next to the last paragraph of which an unnamed investigator of ringworm fungi was contemptuously criticized. The account of this worker's career so accurately identifies a former assistant and collaborator of mine that no one who has known him can help recognizing that the attack was aimed at him. Indeed, a number of readers independently recognized him in the description and spoke to him about it.

Since this work is being done in my laboratory I feel that I should not permit the statements made in this editorial to remain uncorrected. The assertion that the work consists in the collection of cultures taken at random by a technician, from unrecorded cases, is quite at variance with the facts. The investigation was carefully planned after discussion with me. So far it has been confined to the study of a few type strains and their morphologic, biologic and serologic characteristics, in the hope of developing methods for the isolation and identification of other strains. The study of any large number of cases has not yet been attempted. The investigator assailed has had a great deal of experience in experimental work; he has published a considerable number of sound researches, and he has a well established reputation for conservatism and accuracy.

As for neglect of the morphologic features which was alluded to in a supposed quotation from me, I can only say that we still believe that, in a group as pleomorphic as these fungi, morphologic study alone will not lead to clearness. This, indeed, is one of the premises of the experimental plan which is being followed, and this opinion I dimly remember having expressed in ordinary conversation some years ago to the instigator of the editorial, although not in the peremptory form in which I have been quoted.

So much for the work. It is not my intention to burden your readers with an outline of prospective experimental work. The criticism of it and the language in which it is couched are particularly astonishing in view of the fact that neither the investigator himself, nor the undersigned has made any statements about it. No reports have been made at medical meetings, and no notes or papers have been published. The work has hardly been outlined, and the technic is in the developmental stage.

Although we, of course, are always willing to give any information in our possession to any one who comes to this laboratory, there has been so little definite progress in this particular work that no one outside of our laboratory group could possibly have any knowledge of the details. The person, who now admits responsibility for the information given to the writer of the editorial, has not to our knowledge been in our laboratory since this work was begun. The writer whose initials are signed to the editorial has never as far as we know been in the laboratory, is but slightly acquainted with the investigator in question, and is entirely unknown to the undersigned. In consequence, we are entirely at a loss to understand the reasons which could have induced an editorial writer to make a virulent attack on the unpublished work of an investigator of whose plans and methods he had no knowledge whatever.

This, however, is of secondary importance. I am writing primarily to correct the false statements regarding this work and the injustice done to the worker in question. May I add that when this or any other work is published from this laboratory, responsibility for its accuracy and for the conclusions drawn will be partly my own.

HANS ZINSSER, New York.

[COMMENT.—Of course, no one who knows Professor Hans Zinsser or his work can question the reliability of research carried on in his laboratory by an investigator with whom he collaborates, or whose work is conducted under his sponsorship.—ED.]

THE SPELLING OF DERMATOLOGIC WORDS

To the Editor:—One of your humble readers, and perhaps all of them, would like to know which is the proper spelling: leucoderma, leukoderma or leucodermia; leucoplacia, leucoplakia or leukoplakia; leucemia, leucaemia, leukemia, leukaemia or leucocythaemia? While awaiting your official decree the reader above referred to would beg to offer a few comments on the question, not of course with a view to influencing your opinion but merely for what they may be worth.

Uniformity in the spelling of medical words is extremely desirable but unfortunately there are no rigid rules to guide us and common usage is always arbitrary. The question might be correctly answered by quoting the statement of one whose name I do not recall: "You pays your money and takes your choice."

At present there is a tendency toward the curtailment of unnecessary syllables and the elision of diphthongs, which seems to meet with general approval. Anemia and anesthesia are regarded by many as far preferable to anaemia and anaesthesia. The latter spelling may be a trifle more correct, but is certainly less convenient.

The Greek letter kappa usually appears in English words as "c" and the tendency to substitute a "k" is worthy of consideration. Since rhinoceros and keratosis are both derived from the Greek κέρας (keras), a horn, it seems odd that one should be spelled with a "c" and the other with a "k." We spell them so not on principle but from habit. To spell leucoderma with a "c" and leukonychia with a "k," as some of our textbook writers do, is absurdly inconsistent. It is likewise inconsistent to spell leukocythemia with both "k" and "c." It comes from the Greek words λευκός (leukos), white and κύτος (kutos), a cell. If the former word demands a "k," why should not the latter? Consistency would seem to demand either leucocythemia or leukokythemia. But while consistency may be a jewel, it is one which cannot be worn on all occasions. This word might be dropped entirely as its synonym leukemia is shorter and preferable. White blood implies white cell blood.

While either "c" or "k," even used inconsistently, may serve to give us a useful name, I must confess that after changing my opinion several times my present preference is for "k" whenever it is merely a matter of choice. This letter has but one pronunciation which cannot be mistaken, while the letter "c" has two distinct pronunciations. Before "a," "o" and "u" it is like "k" (can, core, cut) and before "e," "i" and "y" it is like "s" (cell, cite, cynic). According to this rule, leucaemia would be pronounced lu-ke-me-a, while with the diphthong changed to "e," leucemia would be pronounced lu-se-me-a.

The Century dictionary gives leucemia, leucoderma and leucoplacia as the proper spelling of these words according to best usage. The Standard gives leucaemia and Webster leuchaemia. In such a matter dermatologists surely have rights which lexicographers are bound to respect. But unfortunately the former do not agree any better than the latter and scarcely two of our recent textbooks use the same spelling for all of these words. Why cannot the American Dermatological Association take up this question and for the sake of a desirable uniformity approve the use of "k" and the disuse of the diphthong or anything else which the members may prefer?

George Henry Fox, New York.

Abstracts from Current Literature

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. VII. A STUDY OF THE NATURAL THERMOLABILE AND THERMOSTABILE HEMOLYSINS AND HEMAGGLUTININS IN HUMAN SERUM IN RELATION TO THE WASSERMANN REACTION. John A. Kolmer, M. E. Trist and A. M. Flick, Am. J. Syphilis **4**:111 (Jan.) 1920.

This article, the seventh of a series by these authors on this subject, is summarized thus:

1. The natural hemolysins and hemagglutinins in human serums may be divided into two varieties, namely, the thermolabile hemolysins and hemagglutinins, those destroyed by heating the serums at 56 C. for thirty minutes, and the thermostabile hemolysins and hemagglutinins, those which withstand this exposure.

2. All natural hemolysins and hemagglutinins in human serums, with the occasional exception of antisheep hemolysin, are destroyed or inactivated by heating the serums at 62 C. for thirty minutes; immune hemolysins and hemagglutinins, such as those produced by injecting rabbits with human cells, are generally more resistant.

3. The thermolabile hemolysins and hemagglutinins in human serums for the erythrocytes of the lower animals are present in groups analogous to the groups of the isohemolysins and isohemagglutinins in human serums; for this reason percentages expressing the presence of natural hemolysins and hemagglutinins based on studies made with the corpuscles of a single animal of each species are only approximately correct.

4. Heating human serums at 56 C. for thirty minutes largely removes the group hemolysins and to a lesser extent the hemagglutinins; thermostabile hemolysins and hemagglutinins do not show the same tendency for grouping.

5. A large percentage of human serums contain a variety of hemolysins for erythrocytes of the lower animals; least is present for human cells, but for the cells of the sheep, ox, guinea-pig, dog, rabbit, rat, chicken and hog, thermolabile hemolysins are present in from 40 to 100 per cent. of serums.

6. Natural hemolysins in human serums for the erythrocytes of persons, rabbits, hogs, guinea-pigs and oxen, are largely of the thermolabile variety.

7. Heated human serums contain lesser amounts of natural hemolysins; that for sheep erythrocytes is most commonly present, being found in from 80 to 95 per cent. of serums; anti-ox hemolysin was found in from 5 to 30 per cent.; anti-guinea-pig hemolysin in from 20 to 25 per cent. and anti-human, anti-rabbit, anti-hog and anti-rat hemolysins in from 0 to 15 per cent. of serums.

8. Natural hemagglutinins in human serums are more resistant to heat than the natural hemolysins.

9. Although heating serums at 56 C. tends to destroy some of the natural hemagglutinins, heated serums yield a higher percentage of positive agglutination reactions than unheated serums due in part to the influence of hemolysins in the latter.

10. Thermostabile hemagglutinins were present in about 95 per cent. of human serums; named in the order of highest percentage present were the hemagglutinins for the erythrocytes of dogs, hogs, persons, rats guinea-pigs, sheep and chickens.

11. There is no relation between the occurrence of hemolysins and hemagglutinins in heated human serums. For example, 90 per cent. of serums contain agglutinins for rabbit erythrocytes and less than 2 per cent. contain hemolysins for the same corpuscles; from 4 to 80 per cent. of serums contain agglutinins for human cells and from 0 to 4 per cent. contain hemolysins. For sheep erythrocytes, however, conditions are reversed as from 80 to 95 per cent. of heated serums contain hemolysins for these cells and only from 4 to 36 per cent. contain hemagglutinins. There is likewise no relation between the occurrence of hemolysins and hemagglutinins in active serums; hemagglutinins for the corpuscles of certain animals of a species may be present and hemolysins absent, or the reverse may be observed.

12. In reference to the Wassermann and other complement-fixation tests, the presence of natural hemolysins and hemagglutinins in human serums are important in relation to the hemolytic system; theoretically at least the presence of a natural hemolysin for the corpuscles of the indicator antigen tends to disturb quantitative conditions in the hemolytic system and reduce the delicacy of the complement-fixation test, while an agglutinin may interfere with hemolysis, particularly with a low titer rabbit immune hemolysin and thereby interfere with the sharpness of the reactions. Judged solely on this basis, human corpuscles are best adapted for complement-fixation tests employing active or unheated human serums; with inactivated or heated serums, human or chicken corpuscles are best suited. Other factors, however, are to be considered before a decision can be made on the best hemolytic system for a standardized technic, namely, the actual rather than theoretic influence of natural hemolysins and hemagglutinins and practical means for overcoming their influence, the ease or difficulty by which immune hemolysins are prepared by injecting the corpuscles of persons and various of the lower animals into rabbits.

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. VIII. THE INFLUENCE OF NATURAL ANTISHEEP HEMOLYSIN IN HUMAN SERA UPON THE WASSERMANN REACTION. JOHN A. KOLMER and ANNA RULE, Am. J. Syphilis **4**:135 (Jan.) 1920.

The authors summarize the article thus:

1. The result of complement-fixation tests with strongly positive serums in amounts of from 0.1 to 0.2 c.c. and an antisheep hemolytic system are not influenced by the presence of natural antisheep hemolysins in the serums; however, serums containing relatively small amounts of syphilis antibody and large amounts of natural hemolysin may yield falsely negative reactions unless the natural hemolysins are removed. In a series of tests this occurred with from 3 to 5 per cent. of such serums.

2. If complement-fixation tests conducted with an antisheep hemolytic system are read immediately after the secondary period of incubation, the influence of natural hemolysins on weakly positive serums in producing falsely negative reactions is not as evident as when the readings are made after the tubes have stood in a refrigerator for sixteen hours or longer.

3. Quantitative complement-fixation tests conducted with varying amounts of patient's serum may be disturbed and rendered inaccurate by the presence of large amounts of natural antisheep hemolysin and particularly with serums containing small amounts of syphilis antibody.

4. While excessive amounts of rabbit immune hemolysin have no influence on the results of tests conducted with strongly positive serums used in amounts of from 0.1 to 0.2 c.c., four or more units of hemolysin may profoundly influence the results of tests with weakly positive serums and with strongly positive serums used in smaller amounts.

5. The removal of natural antisheep hemolysins from human serums by absorption with sheep corpuscles may render some serums slightly anticomplementary but these antilytic substances may be removed by heating the absorbed serums for ten minutes at 56 C.

6. Methods designed for adjusting the antisheep hemolytic system to the natural hemolysins in human serums in order to avoid an excess of hemolysin, have usually increased the delicacy of tests for syphilis antibody. New methods for this purpose are described.

7. The general conclusions of this part of the study are:

(1) The natural antisheep hemolysins in some human serums, and particularly in those containing small amounts of syphilis antibody, may influence the results of complement-fixation tests conducted with an antisheep hemolytic system and yield falsely negative reactions with a small percentage of serums.

(2) These natural hemolysins may be removed by absorption with sheep corpuscles or their influence minimized by special methods, and these means should be employed with practically all serums yielding doubtful or negative reactions to secure best results with an antisheep hemolytic system.

(3) The antisheep hemolytic system is not well adapted for a quantitative complement-fixation test based on the use of varying amounts of patient's serum.

Tomlinson, Omaha.

THE CLINICAL FEATURES AND TREATMENT OF SYPHILITIC AORTITIS. Georg Hubert, Deutsch. Arch. f. klin. Med. **128**:317 (Feb. 18) 1919.

Basing his statements mainly on 220 cases of syphilitic aortitis observed in a Munich hospital during a period of five and a half years, Hubert states that with respect to the pathologico-anatomic changes that occur in this form of syphilitic infection there seems to be general agreement in all essential points, but that as regards the clinical features and the treatment to be pursued, there are wide differences of opinion. The syphilitic origin of the anatomic changes occurring in this type of aortitis has been shown by the discovery of typical gummatous nodular tumors in the media of the aorta. Reuter and Schmorl both found *Spirochaeta pallida* in the wall of the aorta, although, in spite of numerous investigations, their findings have never been verified. In 85 per cent. of the 186 cases in which the Wassermann reaction was taken the result was positive. Tabes was diagnosed in 25 per cent. of the 220 cases. Enlargement of the spleen was noted in 26 per cent. of the cases, which has therefore considerable diagnostic value. In sixty of the cases, the time of the infection could be established. In two cases the first subjective and objective symptoms appeared four years after the infection; in two other cases after five and six years, but in most cases the interval was from fifteen to twenty-five years. The syphilitic infection dated back usually to the second or third decade in the life of the patients. Of the 220 patients, 168 were from 40 to 60 years old when the aortitis was diagnosed. Hubert opposes Jürgensen and also Grau, who place the infection of the aorta in the secondary stage of the syphilitic infection and assume a long period of latency, as he finds no basis for the opinion. Hubert found that syphilitic aortitis constituted 70 per cent. of all cases of syphilis of the thoracic viscera. The relation of the sex incidence of men to that of women was 2:1.

The clinical features depend on the seat, the extent and the severity of the pathologic changes. Early diagnosis is exceedingly important but unfortunately the first symptoms are not marked. In the advanced stages therapy is of little avail. The subjective symptoms are important, as on these often rests the diagnosis and the differential diagnosis with respect to arteriosclerosis. However, subjective symptoms may be entirely lacking, in which case, if the objective findings are positive, and there is a syphilitic history or a positive Wassermann reaction, a diagnosis of syphilitic aortitis should be made and energetic specific therapy should be begun, for it is mainly in such cases as this that there is a prospect of checking the progress of the disease. All subjective symptoms were absent in 35 per cent. of Hubert's cases. In the majority of cases the subjective symptoms are not only present, but even pathognomonic for the disease. Patients usually complain of an uncomfortable pressure beneath the upper margin of the sternum and of a feeling of oppression in the left thorax. In many cases a severe lancinating or burning pain is complained of, usually sharply localized back of the sternum at the level of the second and third rib. The pain is more or less constant but may be increased by physical exertion, rich diet or mental excitement. That the subjective symptoms occur only in complications, as maintained by Benary, Hubert asserts he has disproved by the necropsies of six patients who died of intercurrent diseases. All six patients had complained of severe retrosternal pain and dyspnea on exertion, and necropsy revealed syphilitic mesaortitis without complications. The origin of the pain in aortitis is still in doubt. Hubert assumes irritation of the nerves of the aortic wall. Nearly a third of the patients complained of dyspnea, especially after severe exertion, while a few presented digestive disturbances such as nausea and eructation, which were relieved by specific treatment. Pulsation of the neck vessels, so often mentioned by other writers, Hubert seldom saw. In 50 per cent. of the cases there was a slight enlargement of the heart to the right. Cardiac hypertrophy, though present in 17 per cent. of the cases, was due to renal complications and is not a feature of simple aortitis. Accentuation of the second aortic sound is present in almost all cases and is probably the earliest symptom of aortitis. Over the aorta a systolic murmur is usually heard. These two symptoms, in the absence of high blood pressure, point to syphilis or arteriosclerosis if thickening of the walls of the arteries, mental excitement and exophthalmic goiter can be excluded. Pulse conditions were normal. Blood pressure changes were not marked. Roentgenography, and more especially, fluoroscopy play an important part in diagnosis. In pronounced cases the aorta is distinctly lengthened and distended beyond its normal size. The roentgen findings may be classed among the early symptoms, but the recognition of the earliest pathologic changes in the appearance of the aorta requires considerable experience. If the dilatation of the aorta is not more than 0.5 or 1 cm., one is scarcely justified in speaking of a pathologic condition.

It is often exceedingly difficult and occasionally impossible to differentiate syphilitic aortitis from the arteriosclerotic form. The positive Wassermann reaction, the general condition of the patient and the subjective symptoms will usually be sufficient for differentiation. Aneurysms were present in 16 per cent. of the cases. Their cause is still unknown. In advanced cases the prognosis for recovery is bad, and for life rather unfavorable. If an early diagnosis is made the subjective symptoms can usually be relieved by specific treatment, but the objective findings are seldom much affected thereby. Hubert recommends salvarsan sodium in increasing doses (from 0.15 to 0.45 gm.), and states that frequently all subjective symptoms are relieved by one serial treatment during which from 4 to 4.5 gm. of salvarsan sodium are injected intravenously, but for a completion of the healing process it is necessary to repeat the treatment several times at three to four month intervals. In many cases the Wassermann reaction remained positive after repeated series of treatments in spite of the fact that the disease process had been checked or brought to a standstill. If a negative reaction has been secured by specific treatment and a later reaction is positive, treatment should again be instituted even though there is an absence of subjective and renewed objective symptoms.

H. R. W., Chicago.

PRURIGO EPIDEMIQUE CHEZ LES ASIATIQUES IMPORTES PENDANT LA GUERRE (EPIDEMIC PRURIGO AMONG ASIATICS IMPORTED DURING THE WAR). W. Dubreuilh, Ann. de dermat. et syph. **1**:13, 1920.

Dubreuilh says the importation of colonial workers gave opportunity for observation of a number of unusual diseases, either well-known tropical diseases, accidently imported, or diseases developing in Europe as the result of new living conditions. The cases which he discusses belong in the latter category, and were abundant in 1916, but had almost disappeared in 1917. The patients were all Annamites or Tonkinois, while other Europeans, the negroes, the Africans of the North or Chinese were not affected. The affected men were engaged in various occupations related to the war, and most of the Annamites affected were workers in shops making war materials, or were employed as hospital nurses.

The condition was surprisingly similar in all cases, and at first was considered to be scabies; but the clinical peculiarities, the appearance and distribution of developing lesions, and the failure to find the acarus ruled this out.

The eruption consisted of elevated lenticular papules, identical with those of prurigo and strophulus, and sometimes with a small elevation in the center. Scratched lesions developed a small crust, and disappeared in some days, leaving a brownish stain, sometimes with a central whitish scar. The lesions were always scattered and never grouped, involving especially the lower half of the trunk, particularly in the lumbar region, although they occurred on all parts except the face, hands, feet, genitalia and usually the flexures of the joints. In the intense cases the lesions might become confluent over the lower part of the trunk, leaving a marked, sepia-colored pigmentation. Itching was intense, and was present during the day as well as at night. Adenopathy was marked.

Hospitalization produced rapid recovery, and as a local application a sulphur ointment was used.

Senear, Chicago.

FURTHER OBSERVATIONS ON NEUROSYPHILIS AND THE PSYCHOSES. Lawson G. Lowrey, Arch. Neurol. and Psychiat. **3**:500 (May) 1920.

In this paper the author reports a series of nineteen interesting cases—fourteen of neurosyphilis, one a case of pseudoparesis, and four in which the physical and serologic findings were negative. The clinical symptoms in only four of the fourteen cases of neurosyphilis would justify a diagnosis of neurosyphilis.

The author states that in his opinion neurosyphilis occurs more frequently in association with paranoid psychosis than is usually recognized. Any type of abnormal mental state, or no abnormal state may occur with neurosyphilis. It does not follow that all such cases are paretic. Serologic findings may definitely increase under treatment, with or without increase of clinical signs.

He also says that a negative blood Wassermann reaction, or many such reactions, are not always conclusive evidence that the patient is not a victim of neurosyphilis, nor is a negative spinal fluid evidence of its absence.

He pleads for lumbar puncture in all cases which either present clinical signs of neurosyphilis or which present any atypical features, since neurosyphilis may exist in association with any type of mental symptoms, and since such states may exist without the signs and symptoms of neurosyphilis.

Neurosyphilis as a disease may exist for a long period before symptoms appear.

Oliver, Chicago.

LICHEN PLANUS. E. Graham Little, Brit. J. Dermat. & Syph. **32**:57 (March) 1920.

This article was published in full in The Journal of Cutaneous Diseases **37**:639 (Oct.) 1919.

A CASE OF RECURRENT ULCERATION OF THE SKIN CAUSED BY A DIPHTHEROID BACILLUS. H. W. Barber and F. A. Knott, Brit. J. Dermat. & Syph. **32**:71 (March) 1920.

Barber and Knott record their clinical and bacteriologic observations in a case of recurrent ulceration of the skin which they felt to be due to a diphtheroid organism whose characteristics place it near the upper, or Klebs-Loeffler bacillus, end of the diphtheroid group of organisms.

The active lesions which had existed for some days showed five distinct zones: (1) a red edematous area covered by unbroken skin; (2) a ragged, swollen, bluish-red edge; (3) a thick, yellow adherent slough; (4) a bright red raw surface, covered with granulations; (5) a healing surface with warty projections.

Therapy was unsuccessful until vaccines were used, but after an autogenous vaccine had produced healing, a large dose resulted in a recurrence, and since that time further employment of vaccines and antidiphtheritic serum has not proved efficient.

Senear, Chicago.

PUBLIC HEALTH ADMINISTRATION IN EPIDEMICS OF MEASLES.

John Brownlee, Brit. M. J. **1**:534 (April) 1920.

Children under 6 months do not readily take measles. The greatest susceptibility exists between the ages of 3 and 4 years. Brownlee is convinced that the children of a family are infected at the time the elder children first go to school, where in his opinion the fire of infection most often begins. The death rate between 6 months and 2 years is over 26 per cent., while between 5 and 6 years it is only 4.3 per cent., the average death rate for all cases being 9.1 per cent. In addition, the rousing of a latent tuberculosis is more common in the earlier years. The suggestion is made that schoolchildren in families where there are younger children at home, be sent among adults for the period of the disease rather than to their own homes.

Brownlee considers a rise in temperature nine or ten days after exposure for a single evening to 101, 102 or 103 F. with a fall to normal for from twenty-four to forty-eight hours as the first and most important of the early symptoms. Edema of the palpebral conjunctiva appears as the second symptom. Koplik spots appear late according to Browlee. Hospital care is advised for patients with severe cases and for the treatment of complications.

Goodman, New York.

PEMPHIGUS SUCCESSIF A KYSTES EPIDERMIQUES AVEC SYNDROME ENDOCRINIEN. SES RAPPORTS AVEC L'HEREDO-SPECIFICITE. AMELIORATION PAR LE TRAITEMENT POLYOPOTHERAPIQUE (PEMPHIGUS AFTER EPIDERMIC CYSTS WITH ENDOCRINE SYNDROME. ITS RELATIONS TO CONGENITAL SYPHILIS. AMELIORATION BY TREATMENT WITH POLYGLANDULAR EXTRACTS).

Hudelo and Montlaur, Bull. Soc. franç. dermat. et syph. No. 8, 335, 1919.

Hudelo and Montlaur describe a patient, 10 years of age, who had had an attack of a bullous eruption from time to time through a period of six years. The bullous lesions occurring on the hand and face spontaneously or as the result of pressure, were not inflammatory, and did not itch. Nikolski's sign was marked. The lesions on the hand left atrophic cicatrices with epidermic cysts. Symptoms suggestive of an endocrinous syndrome involving the suprarenals, hypophysis and thyroid glands were present. As the father had syphilis, and the patient dental stigmas and a questionable positive Wassermann reaction, antisyphilitic therapy was instituted but without result. Polyglandular treatment was then employed with striking effect.

Senear, Chicago.

A STUDY OF THE COLLOIDAL GOLD REACTION AND ITS CLINICAL INTERPRETATION.

Margaret Warwick and Charles E. Nixon, Arch. Int. Med. **25**:119 (Feb.) 1920.

From their studies of this test the writers have come to the conclusion that it is the most delicate of the routine spinal fluid reactions, although careful technic is necessary in order to have the proper colloidal gold solutions. It is not to be regarded as a test to replace others but will supplement them as well as have its own value, especially so in the early diagnosis of neurosyphilis. Its supplementary value is especially marked in the various curves which, however, are not specific in themselves as a provocative treatment, but may elicit a curve without other findings. Improvement clinically does not cause improvement in the gold curve although a nonsyphilitic patient has no curve. They state the following interesting conclusions: Clear-cut clinical cases of tabes dorsalis may show all the spinal fluid reactions both before and after treatment: a curve in zone III with a negative cell count and negative or faintly plus globulin is strongly suggestive of a brain or cord tumor or myelitis; curves in zones I and II may be found in nonsyphilitic conditions, such as multiple sclerosis and brain abscess; a cell count above 5 is pathologic. They believe this reaction should be made in all spinal fluid and neurologic examinations.

Jamieson, Detroit.

DIEBETE SYPHILITIQUE ET GLYCOSURIE DE LA PERIODE TERTIAIRE (DIABETES AND GLYCOSURIA OF THE TERTIARY PERIOD OF SYPHILIS). V. Cordier and Dechaume, Ann. de dermat. et syph. **1**:17, 1920.

Cordier and Dechaume review the subject of the association of syphilis and diabetes and report two cases in which syphilitic patients developed diabetes many years after infection. As evidence of the fact that the diabetes was of syphilitic origin, they state that in these two cases the diabetes followed the syphilitic infection, the syphilitic manifestations otherwise were of severe types, the late syphilitic lesions and the diabetes appeared at the same time, increasing or diminishing with equal intensity, and the diabetes was cured by specific treatment alone.

They state that these findings, plus a failure of the diabetes to respond to the ordinary antidiabetic treatment, are necessary before one can say definitely that syphilis is the cause of diabetes in a case where these conditions coexist. The various ways in which syphilis may produce diabetes, and the prognosis in these cases are discussed.

Senear, Chicago.

LATE SYPHILIS OF THE RECTUM. Charles J. Drueck, Am. J. Syphilis **4**:91 (Jan.) 1920.

Late syphilis of the rectum occurs as fibrous hyperplasia, ulcers, and gummas. The latter are usually multiple. Gummas do not form abscesses, but commonly break down forming ulcers and fistulas. The associated proctitis occasions a mucopurulent discharge and feeling of fulness in the rectum. Fibrous hyperplasia may diffuse through all of the rectal structures and lead to multiple ulcerations and fistulas. The pain in such instances is of a burning nature and may be marked.

The majority of nonmalignant strictures of the rectum are syphilitic.

Besides the specific treatment, the most important thing in the treatment of these cases is the prevention of septic infection.

Tomlinson, Omaha.

LE POUMON DES PSORIASIQUES (THE LUNGS IN PSORIASIS). A. Lévy-Franckel and Jacob, Bull. Soc. franç. dermat. et syph. No. 8, 324, 1919.

Lévy-Franckel and Jacob examined by radioscopic means the lungs of fifty patients with psoriasis, and found the lungs normal in sixteen, while twenty-seven showed definite tuberculosis lesions, and six questionable lesions. They do not affirm a toxi-infectious origin for psoriasis, but believe that a tuberculous soil is favorable for the development of the dermatosis.

Senear, Chicago.

A RAW SERUM WASSERMANN TEST EMPLOYING THE SHEEP HEMOLYTIC SYSTEM. J. J. Seelman, Am. J. Syphilis **4**:157 (Jan.) 1920.

The author's technic includes a preliminary titration to determine (*a*) the amount of native amboceptor in each serum and (*b*) the amount of guinea-pig complement to be added to each serum in order to have a standard quantity available for the test, the latter making allowance for the native complement.

These advantages are claimed: It employs noninactivated serum. A sheep hemolytic system is used. Native complement, native amboceptor and nonspecific fixation are allowed for; as a result amboceptor and complement are uniform for all serums in the final test.

Tomlinson, Omaha.

NOTE ON THE "MONOBLOC" OPERATIVE TREATMENT OF TUBERCULOUS LYMPHANGITIS. W. Sampson Hadley, Brit. J. Surg. **7**:324 (Jan.) 1920.

This article is of interest to the dermatologist because the author, after describing the operative treatment in a case of tuberculous lymphangitis associated with verruca necrogenica, states that in his opinion lupus vulgaris is essentially and primarily a lymphangitis of the cutaneous and subcutaneous lymphatics. He bases his belief on observations that the plane of the skin primarily affected (the superficial layer of the dermis) is the plane of origin of the lymphatics of the skin; that changes in the lymphatic vessels of origin can be seen beyond the clinical edge of the area of lupus; and that giant cells are often found in the subcutaneous tissue, usually close to the blood vessels in the situation of the comitant lymphatics.

If lupus is a lymphatic disease, the failure of treatment based on false pathology is not surprising.

Senear, Chicago.

A MORE RAPID AND IMPROVED METHOD OF DEMONSTRATING SPIROCHETES IN TISSUES. Aldred Scott Warthin and Allen C. Starry, Am. J. Syphilis **4**:97 (Jan.) 1920.

The authors give a detailed description of their technic which they say has these advantages: 1. Ordinary formol fixations will give good results. Alcohol fixations also succeed. 2. The sections can be stained singly, on cover-glasses. 3. The time is much shortened, three days being sufficient. 4. Results are more certain than with the Levaditi method.

Tomlinson, Omaha.

THE HEMANGIOMA GROUP OF ENDOTHELIOBLASTOMAS. John Fraser, Brit. J. Surg. **7**:335 (Jan.) 1920.

Fraser has studied a number of hemangiomas from the standpoint of origin, evolution, classification, and histologic characteristics, and concludes: 1. Hemangiomas constitute the most common variety of all tumors encountered during the period of childhood. 2. The tumors are congenital in origin, arising in all probability from "rests" of embryonic vascular tissue. 3. The further development of the tumor leads to the formation of capillary, cavernous and compact varieties. 4. The tumor has striking powers of infiltration, and occasionally it may give rise to metastasis.

Senear, Chicago.

SYPHILIS AS A FACTOR IN ABORTION. Drs. Dougal and Bride, Brit. M. J. **1**:540 (April) 1920.

Of 100 cases the Wassermann reaction was positive in twelve, but in half of these some other abnormal condition was present which might have produced the abortion. In only one case were clinical signs of syphilis present, and in no specimen could typical syphilitic changes or spirochetes be demonstrated. Cases in which syphilis produced the abortion are estimated at not more than 10, and probably nearer 8 per cent.

Goodman, New York.

INTRASPINAL TREATMENT OF NEUROSYPHILIS. G. Marinesco, Rev. neurol. **26**:901 (Dec.) 1919.

Marinesco recites his results after six and seven years in fourteen patients with tabes or paresis whom he treated with salvarsanized serum. Three of the patients with paresis showed apparently good results. One patient, aged 35, served with efficiency as a physician during the war, but recently had a relapse and died insane. The other two patients, one a woman, and the other a man, are in good health eight years after commencing the treatment.

Senear, Chicago.

JUVENILE PARESIS. Edward Livingston Hunt, Am. J. Syphilis **4**:104 (Jan.) 1920.

The author believes there are many cases of juvenile paresis wrongly diagnosed as epilepsy or defective teething.

A complete case report is given with charts of the colloidal gold curve changes. It is shown that this test varies considerably from time to time and that a diagnosis should not be based on one curve.

Tomlinson, Omaha.

BRANCHIOMES CUTANES BENINS (BENIGN BRANCHIAL CYSTS). J. Darier and J. Hallé, Ann. de dermat. et syph. **1**:1, 1920.

Darier and Hallé review the different opinions as to the origin of branchial defects, and enumerate the various types of lesions. They report the case of a girl, 11 years of age, who presented a number of excrescences on the side of the neck which had been present from birth. These extended in a line from the ear to a point 3 inches above the inner end of the clavicle. There were about thirty tumors, some of them bearing a close resemblance to the lesions of molluscum contagiosum. A clear, viscous liquid could be expressed from some of the umbilicated lesions. Histologic examination disclosed malformations which were at the same time verrucous and fistulous, the latter openings leading to cavities with papillomatous vegetations. In diagnosis a linear nevus also had to be considered, but the fistulas ruled this out, while only multiple bronchial fistulas corresponded to the distribution and structure.

Senear, Chicago.

BACILLUS OF THE COLON-TYPHOID GROUP ISOLATED FROM A CASE OF FURUNCULOSIS. W. W. Oliver and Alma F. Schwab, J. Infect. Dis. **26**:336 (April) 1920.

As furunculosis is practically always caused by the *Staphylococcus aureus*, the authors report this case in which a member of the colon group of bacteria was isolated in pure culture from a case of the same.

The marked local and general reaction on the part of the patient following the initial injection of 1 minim of an autogenous vaccine, followed by the patient's freedom from boils for almost two years after the vaccine was administered, suggests a relationship of the bacillus to the disease.

Oliver, Chicago.

LESIONS HISTOLOGIQUES DANS UN CAS DE XANTHOME PAPULEUX GENERALISE (HISTOLOGIC FINDINGS IN A CASE OF GENERALIZED PAPULAR XANTHOMA). L. Spillmann and J. Watrin, Bull. Soc. franç. de dermat. et syph. No. 8, 308, 1919.

Lesions were excised from a 9 year old boy who had generalized xanthoma. Specimens stained with an osmic acid solution showed that two types of fat were present in the xanthoma cells and in the tissue, the first type taking a heavy black stain and soluble in xylene, while the second was stained brownish, and was not soluble in xylene. The patient had a marked cholesterinemia.

Senear, Chicago.

THE USE OF THE PHRASE "WASSERMANN REACTION." John A. Kolmer, Am. J. Syphilis **4**:166 (Jan.) 1920.

Kolmer believes that the use of the term "Wassermann test" should be limited to the test as originally conducted by Wassermann; particularly so in that Wassermann still adheres to his original technic, including the use of salt solution extracts of syphilitic liver as antigen.

The author believes the term "test" should be used to designate technic and the term "reaction" to designate result but that they should not be used as synonymous terms.

Tomlinson, Omaha.

DEUX RECIDIVES DE CHANCRE SYPHILITIQUE DANS L'ESPACE DE SIX MOIS (TWO RECURRENCES OF SYPHILITIC CHANCRES WITHIN SIX MONTHS). Clement Simon, Bull. Soc. franç. dermat. et syph. No. 8, 333, 1919.

Simon's patient developed a chancre on the prepuce, and was given novarsenobenzol. Three weeks after the last injection another chancre appeared at the same site. He was again given the same treatment, but three weeks after the last treatment developed a third chancre. With the first lesion the Wassermann reaction was negative, and there were no other symptoms. With the second lesion he had adenopathy but the Wassermann reaction was again negative, and there were no other manifestations. With the third lesion adenopathy was present and no secondary phenomena.

Simon does not think that this case represents reinfection or a secondary chancriform manifestation, but a recrudescence in situ of spirochetes not destroyed by treatment.

Senear, Chicago.

PARAFFIN WAX FOR FIRST AID TREATMENT IN BURNS. J. R. Garrand, Brit. M. J. **1**:339 (April) 1920.

The suggestion is made to use drippings from ordinary paraffin candles held about 10 inches from the burn as a first aid dressing. The dressing may be completed by putting a small piece of clean linen or absorbent cotton over the wax and dropping more paraffin over it.

Goodman, New York.

CHANCRE DE LA GENCIVE CHEZ UN EDENTE (CHANCRE OF THE GUM IN AN EDENTULOUS JAW). Gastinel and Legrain, Bull. Soc. franç. de dermat. et syph. No. 8, 311, 1919.

Gastinel and Legrain describe the occurrence of a chancre on the upper gum, an unusual location, in a patient who had no upper teeth. He worked in a shoemaking shop where it was the custom of the workmen to fill the mouth with nails, and then to put back in the container those not used. Infection apparently was due to accidental inoculation from this source.

Senear, Chicago.

RADIUM TREATMENT IN FIFTY CONSECUTIVE SKIN LESIONS. Dewell Gann, Urol. & Cutan. Rev. **24**:136 (March) 1920.

As a result of his experience, the writer concludes that radium possesses a definite therapeutic value, and in dermatology it has one of its widest fields of usefulness. It is the method of choice in the treatment of epitheliomas of the skin, keratoses, nevi, pruritus, lupus and warts. It should not be used in the treatment of moles.

Levin, New York

SPOROTRICHOSIS. Legrain and Pellier, Bull. Soc. franç. de dermat. et syph. No. 8, 313, 1919.

The authors report a case of sporotrichosis in which a verrucous primary lesion developed on the nose following a slight injury. There was no local lymphangitis, but ecthyma like lesions were present on the extremities.

Senear, Chicago.

TUBING AS A CAUSE OF REACTION TO INTRAVENOUS INJECTIONS, ESPECIALLY OF ARSPHENAMIN: PRELIMINARY REPORT. John H. Stokes and G. J. Bushman, J. A. M. A. **74**:1015 (April 10), 1920.

The authors believe that in a certain brand of rubber tubing they have discovered a factor that will account for many of the reactions following intravenous medication: Their observations and experiments have resulted in these conclusions:

1. A certain widely distributed brand of so-called pure gum rubber tubing seems to contain when new, a toxic agent responsible for a definite type of reaction following the intravenous administration of arsphenamin, and possibly also of alkaline solutions and transfusion mediums.

2. The toxic substance gradually disappears from the tubing on use.

3. The toxic substance is apparently removable in the first instance by soaking the tubing for six hours in normal sodium hydroxid solution and rinsing.

4. The toxic property is not destroyed in the ordinary process of sterilization by boiling (from one-half to one hour), is not soluble in water or removable by irrigation, appears in toxic amounts in arsphenamin, neo-arsphenamin, and dilute sodium hydroxid solution merely passing them through a new tube en route from container to vein, and is not apparently associated with the mechanically removable debris from the inner surface of the tube.

5. The reaction induced by this agent, as obtained by the use of new tubing for intravenous injection of the substances mentioned, consists of chills coming on from thirty to sixty minutes after injection, with nausea, vomiting, diarrhea, a sharp rise of temperature, sweating, severe headache and lumbar cramps, emotional disturbance amounting at times almost to hysteria, and subsequent profound prostration.

6. The reaction can be induced in a typical form in dogs.

7. The identity and toxicology of the poisonous principle are under investigation.

Waugh, Chicago.

DERMATITIS ARTEFACTA IN THE ARMY. Halden Davis, Brit. M. J. **1**:433 (March 27) 1920.

Davis says that there were few cases of artificial dermatitis in the British forces. He gives Burnier's list of diseases most commonly simulated.

Scabies was imitated by pricking the skin with a needle and rubbing in brine.

Pustular dermatitis was imitated by rubbing in croton oil.

Eczematiform dermatitis was imitated in various ways; sometimes substances were employed such as iodoform or mercury, which act by a special idiosyncracy well known to the malingerer. Other men, not provided with a special idiosyncracy to some drugs, employed ordinary well-known irritants, such as turpentine, petrol, sodium sulphate, etc.

Bullous dermatitis was often produced by the use of blistering plants, found especially among the Ranunculacae and Cruse feral. Chemicals were also sometimes employed.

Abscesses were produced by the insertion of thread, horsehair, or splinters into the skin, and the hypodermic injection of turpentine or petrol. The favorite site of injection was the back of the left hand.

Edema was produced by the use of ligature, usually a broad tape because it was less painful than a narrow one.

Bruises were often produced by repeated tapping with a hard object on the same spot.

The effort to gain a small pension may be the incentive for artificial dermatitis even now when the war is over.

Goodman, New York.

ERYTHEMA NODOSUM AND TUBERCULOSIS. E. Ward, Brit. M. J. **2**:811 (Dec. 20), 1919.

The author states that apart from the mere coincidental occurrence of erythema nodosum and tuberculosis, the condition has been recorded following an injection of tuberculin and under other circumstances in tuberculous patients.

He has also noticed erythema nodosum in tuberculosis when for some reason a chronic condition becomes more acute, or at the time when symptoms of tuberculosis first became noticeable in a patient under observation as a contact case.

Five interesting case reports are given, in all of which erythema nodosum occurred in patients having pulmonary tuberculosis. The author does not suggest that tuberculosis is the only cause of erythema nodosum, but merely that a similar cutaneous manifestation may be due to many different poisons, one of which is that of tuberculosis. The constitutional peculiarity which gives rise to this skin reaction seems to be inherited. In 4,000 cases of tuberculosis and contacts under annual observation, no other skin disorder definitely associated with tuberculosis was noticed, except the well recognized tuberculids. Only a few cases of lupus erythematosus were seen—not more than could be accounted for by coincidence.

Waugh, Chicago.

COMBINED USE OF NOVARSENOBILLON AND MERCURY INTRAVENOUSLY. Reginald Johnson, Brit. M. J. **1**:436 (March 27) 1920.

Johnson employs a mixture of 0.45 gm. novarsenobillon and 2 c.c. of a 1 per cent. solution of mercury perchlorid in a total of 6.5 c.c. injected by syringe intravenously. He says there are several advantages in this combined use of 914 and mercury given intravenously:

1. The mercury gets into the circulation.
2. The method is quick and time-saving as both drugs are given at the same time.
3. Lesions clear up more rapidly than when the drugs are used separately, that is, intravenously and intramuscularly.
4. Stomatitis has not occurred in 100 patients treated. These patients have all received seven injections with 8-day intervals between each injection.
5. In the 100 cases, only two instances of the Jarish-Herxheimer reaction were encountered.
6. At the completion of the course the blood was negative in 95 per cent. of the cases (old tertiary cases were not counted).

Goodman, New York.

THE BIOLOGICAL REACTION OF CARCINOMA CELLS PRODUCED BY RADIUM RAYS. THE TECHNIC OF RADIUM THERAPY IN GYNECOLOGY. Henry Schmitz, Am. J. Roentgenol. **7**:1 (Jan.) 1920.

In this article, with its considerable title, the author does not always discriminate between scientific facts and hypotheses. An interesting discussion, however, is given. Selective absorption of various tissue cells for various rays is taken up.

"The degree of selective absorption of rays by the living cell depends on the particular phase of its life cycle, its species, as well as the age of the host whom it inhabits. Cell elements which are embryonal or undifferentiated are destroyed by a radiation which would cause only a slight reaction in the surrounding mature or highly differentiated cells. The basal cells of the epidermis and hair follicles, lymphoid cells and sex cells (as ova and spermatozoa), are readily killed by an amount of rays which would leave intact the neighboring mature cells.

"Remarkable examples of radio-sensitive tumors are ectodermal and basal-celled epitheliomata derived from the basal-celled layers of the epidermis, lymphadenomata originating from the embryonal lymph cells, sarcomata derived from embryonal connective tissue cells in which the connective tissue fibrillae, cartilaginous and osseous tissues have undergone re-absorption, fibromata in which the fibroblasts are present in large numbers and do not develop into highly differentiated adult cells, and connective tissue fibers.

"On the other hand squamous-celled epitheliomata, fibrosarcomata, chondrosarcomata, osteosarcomata, and fibromata in which atrophic fibroblasts and abundant fibrous tissue have been retained, are very refractory to radiation."

Elbert Clark, Chicago.

A CASE OF TUMOR-LIKE CHANCRE OF THE THIGH. A. M. H. Gray, Brit. J. Dermat. & Syph. **32**:37 (Feb.) 1920.

Gray describes an unusual primary lesion in a girl, aged 20, who stated that this lesion began two months before as a small spot, which had slowly and regularly increased in size to its present dimensions.

On examination an oval swelling was seen on the front of the left thigh at the junction of the upper and middle thirds; it measured 4.5 by 3.75 cm., and was raised 6 or 7 mm. from the surrounding skin. The margin of the swelling rose abruptly from the skin, while the summit was hollowed out into a wide saucer-shaped depression, as shown in an accompanying photograph. Surrounding the base of the tumor was a sharply-defined, hard, collar-like band, about 1 mm. wide and of the same height; it was of dead white color. The tumor itself was of purplish color, was elastic to the touch, and had a glistening smooth surface except for a small area in the central depression, which was covered by a thin crust. There was no sign of moisture over the general surface of the tumor.

To judge by the literature, hypertrophic chancres are distinctly uncommon, especially when they attain such a size as in the case reported above. Ulcerating and fungating chancres of considerable size have been frequently described, but these smooth, dry, tumor-like chancres are apparently of much less frequent occurrence.

The character of the chancre is determined in part by two factors: freedom from damage to the surface and absence of secondary bacterial infection, and it is because it is so rarely possible to prevent these two accidents from happening that this type of chancre is so infrequent.

Senear, Chicago.

A METHOD OF TREATMENT FOR NEUROSYPHILIS. John A. Kolmer, J. A. M. A. **74**:794 (March 20) 1920.

The author criticizes the Swift-Ellis system of intraspinal therapy of neurosyphilis because of the minute amounts of arsphenamin detectable, such as arsenic, carried over in serum secured by drawing blood one hour after the intravenous injection of arsphenamin. The objection is removed by the technic of Ogilvie, who adds arsphenamin, and by that of Marinesco, who adds neoarsphenamin, to serum *in vitro* prior to intraspinal injection; but in both methods the patient may be deprived of the beneficial effects of the intravenous administration of these drugs, which probably constitutes a valuable part of the Swift-Ellis treatment. Kolmer uses a plan of combined mercury and arsphenamin treatment by which he believes these objections are corrected. The course of treatment covers a period of four weeks, during which twenty-four inunctions of mercury, 360 grains of potassium iodid and four combined intravenous and subdural injections of arsphenamin are given. The author gives a detailed description of the technic used in the combined intravenous and subdural injections which require two hours for the procedure.

The advantages claimed are:

1. The patient received arsphenamin both intravenously and intraspinally.

2. Blood is removed at once, insuring in the serum a larger amount of arsphenamin than is secured after an interval of an hour, as in the Swift-Ellis method.

3. Plasma or serum is secured at once, rendering the complete treatment possible within two or three hours instead of an interval of over night between the intravenous and intraspinal treatments.

4. The removal of from 20 to 30 c.c. of cerebrospinal fluid, followed by the injection of but 10 to 12 c.c. of arsphenamized serum, very probably leaves cerebrospinal fluid pressure reduced for some time, producing increased vascularity of the cord and probably also of the brain, with the beneficial effects ascribed alone to spinal drainage. Indeed, injection of arsphenamized serum within an hour of intravenous injection may increase extravasation from the meningeal vessels by reason of irritation produced by the serum and arsphenamin in the subarachnoid space, in addition to the increased vascularity and transudation ascribed to reduction alone of cerebrospinal fluid pressure.

5. The patient receives the benefit of treatment with mercury and iodids and of spinal drainage conducted while under the influence of these antisyphilitic medicinals.

Waugh, Chicago.

SYPHILIS HEREDITAIRE ET DYSTROPHIES (Continued). V. Hutinel and H. Stevenin, Arch de méd. d. enf. **23**:77 (Feb.) 1920.

In this paper, Hutinel and Stevenin continue the discussion of the various dystrophies of hereditary syphilis, and a major portion of the article is given over to a discussion of the dystrophies of special parts.

They also consider the association of hereditary syphilis with other diseases. They have noticed that incidental infections or intoxications often excite latent syphilitic foci in certain organs. Conversely, they feel that the lowered resistance provided by syphilis often determines the localization of attack on certain organs, especially the brain, liver, pancreas and suprarenal glands, by such diseases as scarlet fever, diphtheria and typhoid fever.

They state that the effects of a chronic infection such as syphilis, can be intensified by an acute disease, and that likewise the acute disease may be given unusual severity in a syphilitic due to the presence of a chronic disease.

This reciprocal effect is most marked, however, when we have two chronic diseases occurring in a single patient. A patient with hereditary syphilis. acquiring tuberculosis, shows a particular tendency to develop sclerous lesions, and the lesions can be modified by specific treatment. Likewise, when a tuberculous patient acquires syphilis the tuberculous process is apt to become less severe.

Senear, Chicago.

TARDY OSTEOPERIOSTITIS WITH INHERITED SYPHILIS. A. Varisco, Riv. Crit. di Clin. Med. **20**:505 (Oct. 25) 1919.

Varisco reports a case in which inherited syphilis first manifested itself as osteoperiostitis at 20 years of age. The patient was an apparently healthy young woman. The history showed no illness, except a few convulsions in infancy, and measles at 18. There was nothing to suggest inherited syphilis in the case except the shape of the patient's teeth. At 20 she developed pain in the legs, and pain and swelling of the large joints, with a low fever; the spinal fluid was normal. After six months the symptoms subsided so that she could leave the bed. After a few months more painful nodes developed in the crest of the tibiae, in other long bones, and the clavicles. Nearly a year after the beginning of the illness, under a tentative course of mercury the diagnosis cleared up, previously negative Wassermann reaction became positive, and a clinical cure resulted.

Pusey, Chicago.

TOXIDERMITIS MEDICAMENTOSA. U. de Nonohay, Arch. Rio-Grandenses Med. **1**:21 (Jan.) 1920.

After a review of the accidents observed as a consequence of the injection of arsenic salts, the author refers to the disturbances of the internal secretions—especially of the suprarenals—which are perhaps produced by syphilitic infection and not by the arsenic, as has been suggested. He concludes that arsphenamin salts in the treatment of syphilis should be used with care, and epinephrin or several doses of mercury should be given before its injection. He does not believe that the reactions are due to impurities in the water or in the sodium chlorid of the normal solution used by some physicians, adding that impurities, if they exist, are negligible. He concludes with the statement that preparations of arsphenamin are always harmless if used carefully and after a thorough examination of the patient.

Pardo-Castello, Havana.

ZUR VACCINETHERAPIE DER FERUNKULOSE. Prof. Hans Schirokauer, Therap. d. Gegenw. **10**:397 (Oct.) 1919.

The author relates briefly his experience with, and opinions of, vaccine therapy in furunculosis. In acute staphylococcic infections the results of vaccine treatment have not been commendable; in obstinate chronic cases the results were highly favorable.

The best results were obtained in a series of nineteen obstinate cases. These were of from one to three years' standing and were contracted during the war. Most of the patients had had various internal treatment, including arsenic and yeast. Commercial vaccines were used. Injections were intramuscular; 100 million staphylococci were usually given at the first dose. If there was no reaction the treatment was repeated the next day. The injections were then given twice a week in increasing doses up to a dosage of 1,000 million. Sixteen of the nineteen patients have completely recovered; three are much improved.

Elbert Clark, Chicago.

PURPURA ANNULARIS TELANGIECTODES. Prof. G. Verrotti, Riforma med. **36**:145 (Feb. 7) 1920.

Professor Verrotti describes a peculiar case of Majocchi's disease confined to the hypogastric region, in a woman 40 years old. The cutaneous lesions were discovered when the patient was examined by a gynecologist for an abdominal tumor which proved to be a fibroma of the uterus. The dermatosis was confined to those areas of the skin in which the nerves were irritated by the pressure exerted by the tumor. After the removal of the latter, the cutaneous lesions disappeared. The author thinks that the nervous disturbance caused by the tumor was the only etiologic factor in this case. He refers to another instance of the same disease in a woman 42 years of age who suffered from deficient ovarian secretion. Genital disturbances as possible etiologic factors should be kept in mind in cases of purpura annularis telangiectodes occurring in women.

Pardo-Castello, Havana.

ALTERATIONS DES AMPOULES D'ARSENOBENZOL ET DE GALYL HUILEUSES ET GLUCOSEES POUR INJECTIONS INTRAMUSCULAIRES. F. Balzer, Bull. Soc. franç. de dermat. et syph. **7**:290, 1919.

Balzer states that the color changes taking place in oily and glucose preparations of arsenobenzol and galyl, designed for intramuscular use, do not as a rule indicate that the toxicity of the drug is increased, and he says further that preparations which have taken on a brownish color are less painful. He recognizes, however, that such color changes render the drug unsafe for intravenous use. Darier, in discussing the paper, summarized Balzer's statements well by saying that Balzer's communication does not prove that changes in arsenobenzol are unimportant but that the solutions are dangerous for intramuscular use.

Senear, Chicago.

THE EFFECT OF WEAK ACETIC ACID ON SPIROCHAETA PALLIDA. Herman Goodman, J. A. M. A. **74**:803 (March 20) 1920.

The author gives a preliminary report of the clinical and experimental evidence regarding the effect of weak acetic acid on *Spirochaeta pallida.* When using the solution to hemolize blood in the attempt to remove the spirochetes, the organisms were much changed, had lost their coil and were immotile. The author believes that the spirochete is unable to live in an acid environment and that such an environment might be of use in the prophylaxis of syphilis. He intends to carry on the investigations on animals, and to determine whether the acetic acid penetrates more deeply into tissue such as the mucosa than solutions of other local spirocheticides.

Waugh, Chicago.

ACUTE SYPHILIS OF THE KIDNEY. H. N. Cole, Am. J. Syphilis **4**:46 (Jan.) 1920.

Acute syphilis of the kidney is a rare disease. Fournier's criteria for diagnosis were (1) proof of a recent syphilitic infection, (2) appearance of a nephritis with syphilis, (3) lack of other sources for the nephritis, (4) striking characteristics of a nephritis: (*a*) a high albumin content in the urine, (*b*) a rapid onset of the kidney disease, (*c*) a tendency to early uremia.

To these might be added (1) a positive Wassermann reaction, (2) weakness and loss of weight, (3) striking edema, (4) presence of spirochetes in the catheterized urine, and (5) influence of specific therapy.

The author reports a typical case which satisfies these demands.

Acute syphilitic nephritis is often fatal.

Tomlinson, Omaha.

NEUROLOGICAL JOTTINGS. James Taylor, Brit. M. J. **1**:282 (Feb. 28) 1920.

Taylor reviews the interesting relation between herpes zoster and chickenpox, and gives the points common to all the cases of a series:

1. Chickenpox in one person followed shingles in another in the ordinary incubation period of chickenpox.
2. No other source of infection was discovered.
3. Chickenpox in a child followed an attack of shingles in an adult.

Shingles and chickenpox may coexist in the same patient, or cases of both in different patients living in the same house.

Goodman, New York.

CEREBRAL SYPHILIS. Luis Guedes, Arch. Rio-Grandenses Med. **1**:19 (Jan.) 1920.

Guedes presents a case of cerebral syphilis which had been clinically diagnosed as dementia praecox. On account of the age of the patient (36 years) the presence of gland enlargement and of increased patellar reflexes, several laboratory tests were made, giving a positive Wassermann reaction, both in the blood and the spinal fluid, moderate lymphocytosis and increased albumin. Specific treatment was instituted and the patient made an uneventful recovery.

Pardo-Castello, Havana.

MULTIPLE PIGMENTED HEMORRHAGIC SARCOMA (?); A CASE FOR DIAGNOSIS. E. G. Graham Little, Proc. Roy. Soc. Med. **13**: 13 (Dec.) 1919.

A gardener who had used an arsenical spray for many years presented a condition described as confluent telangiectases involving the dorsum of both hands and all of the palmar surfaces except a small patch in the center of each. The skin surface, being a deeply suffused brick-dust color, was smooth and unaltered. There was a distinct brownish pigmentation. The nails were thickened. Subjectively a burning sensation was noted. The diagnosis was in doubt, Kaposi's sarcoma, lupus erythematosus and an unusual type of arsenical dermatosis being considered. It was considered significant that other growers in the same district were reported to be similarly affected.

Guy, Pittsburgh.

ANAPHYLAXIS TO ACETYLSALICYLIC ACID. F. Widal and P. Vallery-Radot, Presse méd. **28**:93 (Feb. 4) 1920.

Widal and Vallery-Radot report an interesting case of cure of anaphylaxis by acetylsalicylic acid. The patient had suffered from the condition for nine years. The treatment began by the administration of the drug tonic in doses of 0.005 gm. at an interval of an hour, then at a similar interval 0.25 gm. twice and finally 0.5 gm. twice. This was repeated thirteen times in six weeks, the preliminary dose being increased from 0.005 gm. to 0.03 gm. A complete cure resulted.

Pusey, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, March 2, 1920

JOHN E. LANE, M.D., *Chairman*

CULTURE FROM CASE OF RINGWORM OF THE NAILS. Presented by DR. HOWARD FOX.

Dr. Fox gave a demonstration of culture from a case of ringworm of the nails previously presented. The culture medium, 4 per cent. glucose agar, showed a trichophyton though the type could not be identified, as Saboraud's medium was not obtainable. The culture was made at the Laboratory of the Vanderbilt Clinic.

CASE FOR DIAGNOSIS. Presented by DR. WISE.

Harry M., from Dr. Fordyce's service, aged 51, single, was born in the United States, and stated that the duration of the condition was four years. There was a lesion on the flexor surface of the right index finger, between the first and second phalanx, which was crusted with a transverse rhagade about half an inch wide, showing a suspicious rolled edge. He had been treated with the roentgen ray about two years before. He gave a doubtful history of syphilis seventeen years ago.

DISCUSSION

DRS. HIGHMAN and PISKO thought the condition was epithelioma.

DR. TRIMBLE also regarded the ulcer on the finger as an epithelioma. He was, however, particularly interested in the keratosis on the palm and fingers and wondered whether the man had been taking arsenic in any form. He had previously observed an epithelioma developing on a keratosis produced by arsenic.

DR. MACKEE agreed with the diagnosis of epithelioma. There were numerous keratoses and small epitheliomas on the face and many keratoses on the hands. The skin of these parts was of the senile type. The general picture was that of a man who had an idiosyncracy to sunlight—sailor's skin.

DR. WISE said there had not been time to study the case but if anything definite was learned later the patient would be presented again.

HERPES SIMPLEX OR ZOSTER WITH PSORIASIS. Presented by DR. ABRAMOWITZ.

Vincent C., from the Vanderbilt Clinic, was 10 years of age. He was born in the United States and had had psoriasis on and off for seven years. The eruption exhibited on the right side of the face had been present for three days and was preceded by pain in the left jaw, from which a tooth had been extracted. The eruption consisted of vesicles and bullae on an erythematous base, and covered the entire cheek, upper and lower lip on the left side.

DISCUSSION

Dr. Levin said that in view of the fact that we are just passing through an epidemic of lethargic encephalitis, the boy should be watched for the possible development of that disease. Some cases of the disease appeared with neuritis and herpes as prodromal symptoms. There was also a history of nausea, vomiting and coryza occurring two days prior to the appearance of the herpes.

LYMPHO-GRANULOMA OF THE SCALP IN HODGKIN'S DISEASE.

Previously presented by Dr. Howard Fox at the New York Dermatological Society, February 24. Diagnosis confirmed by microscopic report of Dr. Highman.

DISCUSSION

Dr. Fraser said that lesions presenting the typical picture of Hodgkin's disease were of rare occurrence in the skin. He believed that the majority of cases reported as such were lesions of the subcutaneous lymphoid tissues rather than of the corium. He had observed only one case in which the typical Hodgkin's lesion was present in the true skin. This was a case in Dr. Trimble's service at Bellevue Hospital. Sections taken from the skin showed in the upper part of the corium lymphocytes, large endothelioid cells, and a few of the large multinucleated cells which since the publication of Dr. Dorothy Reed's work have been regarded as the cell typical of Hodgkin's disease.

The case presented by Dr. Fox appeared to the speaker to be interesting from the standpoint of its analogy to mycosis fungoides. The dermatosis present resembled that found in the latter disease more than that described as usually occurring in Hodgkin's disease. He recalled a case of mycosis fungoides which he had reported a few years ago before the Section on Dermatology of the American Medical Association. In this case the skin lesions bore a striking resemblance to the histologic picture found in Hodgkin's nodes, and the picture in lymph nodes removed at necropsy might well have passed for the late sclerotic lesions found in that disease. It would be interesting to know the histologic picture in the present case, though of course absence of the typical picture in the skin would not exclude the diagnosis of Hodgkin's disease as the majority of dermatoses associated with the disease do not show the histologic features found in the lymph nodes. Gordon Ward, in discussing this subject at a meeting at the Dermatological Section of the Royal Society, referred to a typical case of Hodgkin's disease in which all the organs of the body except the skin presented a typical histologic picture.

In Dr. Fox's case the red blood count was practically normal. In Hodgkin's disease one would expect to find a picture of anemia. The case should be studied further and carefully observed, and sections of the skin should be studied histologically before a definite conclusion as to its nature could be reached.

Dr. Fraser reiterated his conviction that the dermatosis in this case was not that usually found in Hodgkin's disease.

Dr. Highman expressed regret at being obliged to disagree with Dr. Fraser. He had seen the patient in Dr. Fox's office by daylight. The condition impressed him then as being either a leukemia or Hodgkin's disease, unless it were a rare form of mycosis. In true mycosis, one would expect a history of a prefungoid rash. Mycosis did not involve the scalp as frequently as leukemia and pseudoleukemia. In fact, scalp and face involvement were among the recognized features of this disease, however rare.

Dr. Highman said that he thought the condition was probably not a mycosis. The question was whether it was a true leukemia in the aleukemic or subleukemic phase, or whether it was Hodgkin's disease. In discussing a group of which so little is known, it was difficult to express any strong convictions; nevertheless, based on the purely subjective foundation—which unfortunately was so common in dermatology—the case impressed him clinically as more likely to be the one of leukemia than mycosis. The report that the typical glandular structure of Hodgkin's disease was found supported that assertion. He had examined a piece of the scalp lesion at the Vanderbilt Clinic, and found "an infiltration filling the papillar body which could be separated into two elements; in one, surrounding the larger capillaries, are islands of pure lymphocytes, representing a local infiltration around the vessels; these lie embedded as islands in a more diffuse infiltration of larger cells which must also be classed as lymphocytes. There are a few eosinophils, and at least one example typical of the Dorothy Reed body."

These findings convinced him that the case was Hodgkin's disease. That the patient had a condition of lymphogranuloma was certain. It might be leukemia or mycosis, but his personal bias was in favor of Hodgkin's disease.

Dr. Trimble agreed with the diagnosis of the case as presented. As he recalled his own case, to which Dr. Fraser had referred, it did not resemble this one closely. The lesion was on the side of the neck and looked like the flat type of lupus vulgaris. It was deeply infiltrated and had a copper-colored hue. According to the patient's statement, the lesion began following the removal of a gland in the neck; and on examination it turned out to be of the same structure as a lymph node, so there was no doubt of its being a case of Hodgkin's disease of the skin. It was similar to a case reported in an article by Dr. Cole of Cleveland, who classified the lesions in two groups, the last group being the granuloma type.

Dr. Levin said that the case reminded him of one shown by the late Dr. Gottheil from the City Hospital in 1915. The patient, Hugo Lutzenberg, presented a lesion on the scalp much like this one except that the skin was more edematous and elevated. Microscopic examination proved it to be mycosis fungoides. It was difficult to see how it was possible clinically to make a positive differential diagnosis between Hodgkin's disease, leukemia, mycosis fungoides and other allied conditions. In view of the microscopic findings in the case presented, he thought the diagnosis of Hodgkin's disease should be accepted.

Dr. Fraser said that since Dr. Highman had explained the finding of the characteristic picture in the skin lesions he was willing to accept the diagnosis of Hodgkin's disease; the so-called Dorothy Reed cell was typical of the condition and, so far as he was aware, was not found in any other condition. He repeated, however, what he had said before, that typical lesions of the true skin are rare in Hodgkin's disease; and he believed that many of the cases that had been reported as nodules in the skin were not lesions in the true skin at all, but nodes of the subcutis. One of his own cases had illustrated this point very well. The nodes in certain places were adherent to the true skin, but when removed microscopically they proved to be lymph nodes in which the normal architecture was replaced by the typical picture of Hodgkin's disease. The case presented by Dr. Fox was a most interesting one and should be recorded in the literature as one showing the typical Hodgkin's lesions in the skin.

Dr. Highman, referring to Dr. Levin's remarks, said that he recalled Dr. Gottheil's case. Although it was presented as mycosis, many did not accept it as such. As to differentiating among these cases, he wished to say that though the majority of observers find it difficult, few find it impossible. He referred Dr. Levin to articles by Arndt, Audry, Fraser, and Paltauf, which might point out to him that recognition of these maladies is not without the realm of possibility.

Dr. Fraser, in response to a request from Dr. Wise, drew a picture of the Dorothy Reed cell on the board and explained that it was a large cell, with sometimes only one, but in the majority of cases several, nuclei which are characteristic. These cells usually have pale staining nuclei with deeply staining nucleoli.

Dr. Howard Fox said that in Dr. Cole's paper, to which Dr. Trimble had referred, two classes of skin lesions were observed in connection with Hodgkin's disease. The first class included prurigo-like eruptions, urticaria, pruritus, pigmentation, and dermatitis exfoliativa, which were of an inflammatory nature and probably toxic in origin. The second class consisted of infiltration and tumor-like lesions which showed the definite histologic structure of a lymphogranuloma and were infrequently observed.

TINEA FAVOSA. Presented by Dr. Levin.

A boy, aged 7, born in this country, presented lesions of the scalp which had been present for more than a year. Covering the whole scalp, there was a thick layer of dirty yellow and grayish crust which was firmly adherent to the underlying inflamed scalp. The condition was most marked over the anterior two thirds of the scalp, on which were several irregular areas showing a loss of hair. A distinct musty odor could be detected. Mycelia and spores were present in the crusts and hairs.

MATCH-BOX DERMATITIS. Presented by Dr. Levin.

S. E., a married man, aged 45, a cloak-maker, presented himself two weeks before for treatment of a lesion which had been present on his left thigh for three months. It then covered an area about 5 inches in diameter on the anterior surface of the left thigh, corresponding to the region of his left front trouser pocket. The lesion was dark red, elevated, superficial, crusted, and vesicular. On investigation, it was found that he had for several years carried boxes of matches in the left pocket—never on the right side. There was no lesion on the right thigh. He was advised not to carry matches in his trouser pocket and was treated with Lassar's paste. When seen three days ago the eruption was practically gone, and he was asked to begin carrying matches in the trouser pocket again.

DISCUSSION

Dr. Williams said that it was a most interesting case, one that was not ordinarily observed, but that he had seen two such cases in camp in which the men carried their matches in the trousers' pocket and showed the same kind of lesions except that they were more papular and not quite so extensive. Both cases cleared up by the removal of the matches. It was an excellent illustration of the so-called eczema cases; the more we learn of them, the more eczema shrinks.

Dr. Highman said that he had seen other cases and that this one was typical.

MILIARY PAPULAR SYPHILID, ASSOCIATED WITH PALMAR AND PLANTAR KERATOMA. Presented by Drs. Chargin and Abramowitz.

A. W., aged 22, from the Chelsea Venereal Clinic, was a Canadian seaman who contracted a penile chancre about three months before, for which he received local treatment only. The eruption presented first appeared on his face ten days before and spread rapidly all over the body. The eruption on the face was an erythematous dermatitis involving the follicles on bearded and nonbearded regions, also the upper part of the neck. There was moderate scaling and smarting of the face was complained of. Fading macules were present on the trunk and extremities. The follicular eruption was mainly on the interscapular region, the outer ends of the extremities, buttocks and dorsum of first phalanges, and consisted of pinhead and larger papules, some with depressed centers, others capped with scales. The eruption on the hands bore a close resemblance to pityriasis rubra pilaris. There was a marked keratoderma of the palms and soles, in the former area being associated with erythema and minute papules noticeable at the edge of the lesion. The lesions on the hands and feet had been present as long as the patient could remember. The inguinal glands were markedly enlarged, but there were no mucous membrane lesions. In the intergluteal region was an eruption similar to that on the face, but about the size of a silver dollar. The Wassermann reaction was ++++.

DISCUSSION

Dr. Wise inquired whether the patient had taken either mercury or arsphenamin before the eruption appeared, and expressed the opinion that the lesions were not all syphilitic. The eruption on the back of the neck was not a follicular syphilid. It seemed that there were two rashes, a syphilitic one and a superimposed follicular rash of different origin, probably Devergie's disease.

Dr. Williams expressed his appreciation of an opportunity to see such a case. One noticeable feature was that a syphilid with papules so extensive as these should remain so pink; only three or four of the lesions had sunk to the ordinary brownish tint. It was a remarkable case.

Dr. Highman agreed with Dr. Wise that there were two conditions in the case, and expressed the opinion that one was pityriasis rubra pilaris of Devergie.

Dr. Howard Fox thought the entire eruption was syphilitic. It was similar to a case of miliary papular syphilid resembling pityriasis rubra pilaris that he had reported. Although he felt sure of the diagnosis of syphilis, he thought the lesions on the arms and hands imitated to an extraordinary degree the lesions of Devergie's disease, with the acuminate scaly papules and thickened palms.

Dr. Abramowitz said that the eruption was a little brighter and more reddish than it was the day before when the patient was first seen. At that time, they were uncertain whether it was a purely syphilitic rash or a syphilitic rash accompanying some other condition. Some of the lesions on the face, back and extremities resembled a case of pityriasis rubra pilaris. The penile lesion had received some local treatment, but no arsphenamin was given. The eruption presented was of eight or ten days' duration. In the morning, the man had had his first mercury injection, and it had evidently irritated the lesions. The condition was probably syphilitic.

CHRONIC ECZEMA WITH LICHENIFICATION. Presented by Dr. Williams.

I. H., aged 59, married and a novelty salesman, had applied for treatment at the Skin and Cancer Hospital. His previous and family history were negative, and the condition for which he was presented had lasted for six years. The flexures were first involved, the lesions being flat, shiny, skin-colored papules, with mild itching. Later the inner surfaces of the thighs and legs became affected, the eruption finally covering the whole body with the exception of the hands and feet. The lesions were essentially small flat or rounded, generally smooth, pale pink papules which showed marked excoriations resulting from scratching. There were also many enlarged sebaceous glands on the forehead and over the sternum. Pathologic report: chronic eczema.

PRURIGO NODULARIS. Presented by Dr. Williams.

(Previously reported: *Jour. Cutan. Dis.* **32**:461, 1914; *Am. Jour. Med. Sc.* **150**:392 [Sept.] 1915; *Jour. Cutan. Dis.* **34**:380 [May] 1916.)

Miss S. O., aged 30, was of Swedish ancestry. There was nothing of importance in the family or personal history. The hair had always been thin. The skin was coarse and harsh and did not chap easily; it blistered easily from moderate heat, and developed callosities easily.

The present disease began in the summer of 1911 with a series of boils on the forearms and papules which itched intensely. Ordinary hives had not been noticed. The papules occurred on both forearms, hands, legs and feet, with a few scattered lesions on the arms and thighs. Lesions had been observed on the tongue. Lesions once formed persisted indefinitely and disappeared slowly or not at all.

DISCUSSION

Dr. Williams said that these two cases made a good pair to two others reported by him some years ago and published in the *Am. Jour. of the Med. Sciences.* One man had a chronic pruritic condition of the skin; there had been no vesicles and no tendency to grouping, but the lesions were scattered diffusely and the itching was intense. The papules resembled lichen planus and were chronic itching papules, but the microscopic picture was not at all that of lichen planus. The condition was aggravated by scratching, and if that could not be checked the man would probably develop papules and nodules. There were already distinct patches of lichenification on the thigh.

The other patient with prurigo nodularis exhibited a leathery skin on the hands and forearms, but in this case the nodules came first and the itching later. In the man there might be a small nodule, but the itching came first, then he scratched, and later developed the nodules.

One condition was a pruritus which was scratched, the other an itching papule. Dr. Williams said that if any one could suggest a better name than chronic eczema or chronic pruritus for the first case, he would be glad to accept it.

Dr. Pisko suggested calling the first case eczema pruriginosum.

Dr. Howard Fox said he could not agree with Dr. Williams. If the lesions in this case were not more or less grouped, then his conception of the word differed from that of Dr. Williams. The patient presented a chronic, extremely itchy, relapsing eruption of papular lesions that in his opinion were grouped. He felt that the case could probably be classed as one of Dühring's disease. That there were no vesicles did not lessen the probability of this diagnosis, as many cases of this disease were of a papular rather than vesicular or bullous type.

Dr. Highman said he was less interested in the designation than in what caused it. One feature that had impressed him as interesting was that the man had general adenopathy. The old Viennese school recognized a type of preleukemic disease, prurigo lymphatica. It would be interesting to study this case clinically to find whether it did not prove to be a forerunning stage of leukemia.

Dr. Trimble expressed his interest in the case of the man and in Dr. Highman's statements regarding it. If the same lesions had occurred in a child of 6 or 7, most physicians would have said immediately that it was prurigo. He could not conceive of any one as old as this patient having prurigo. It would probably have to be accepted as a case of dermatitis herpetiformis of the papular type. He then recalled the case of a young woman of 18 who presented similar lesions that were pronounced to be prurigo; the patient asserted that she had never had any vesicles. The lesions were not grouped, though the condition had started at 6 and continued for twelve or fifteen years. While under observation in the City Hospital, she developed grouped vesicles, and a diagnosis of dermatitis herpetiformis was made.

Dr. Williams thanked Dr. Highman for his diagnosis of possible leukemia or pseudoleukemia, and was also pleased to have Dr. Fox's suggestion of dermatitis herpetiformis, though he could not agree with it. The lesions did not seem to show the close grouping, though they were thicker in some parts of the body than in others. The soft swelling of the skin and the congestion found in groups of dermatitis herpetiformis was not found and for that reason the diagnosis could not be accepted, although it had been considered. Whether the condition was called neurodermite or prurigo was largely a matter of words.

LUPUS VULGARIS. Presented by Dr. Bechet.

A woman, aged 48, from Dr. Trimble's service at the University and Bellevue Dispensary, stated that she had first noticed the eruption fifteen years previously. The entire forehead was covered with an infiltrated brownish red plaque, with here and there a healed scarred area an inch or more in diameter. This diseased area ended symmetrically at both temples. Over the nose and on either side of it, extending over the malar regions, was a more recent patch; this was also retrogressing over the nose, leaving an atrophic shrunken scar. At the periphery of this lesion were a number of papules and tubercles which on pressure with the diascope revealed the characteristic "apple jelly" nodules. There was some ectropion of the left eye. The patch occupied the "butterfly area" of the usual case of lupus erythematosus, and being rather superficial bore a slight resemblance to the latter. The case was presented because of its unusual distribution.

BROMODERMA. Presented by Dr. Wise.

Mary G., 6 months old, was brought by her mother—who was free of dermatoses—to Dr. Fordyce's service at the Vanderbilt Clinic. The duration of the eruption was three weeks, previous to which the baby was given bromids for one week. On the scalp and gluteal region were pustular and papular lesions closely grouped, which formed a granulomatous mass about the size of a hazelnut.

LEPROSY (NODULAR TYPE). Presented by Dr. Wise.

Jeanette J., a widow, aged 55, was born in the United States and had always lived here. The duration of the condition from which she suffered was one year. The eruption consisted of nodular masses, split-pea and kernel sized, on the eyebrows and eyelids. On the trunk and extremities, dollar-sized depigmented and anesthetic patches were present.

ACNE VARIOLIFORMIS. Presented by Dr. Howard Fox.

A mulattress, 25 years of age, born in the United States, and married had an eruption that had been present on the forehead and scalp for the past eight months, and on the nose for the past three months. She complained of moderate itching. She had had no miscarriages, and the Wassermann reaction was negative. The eruption consisted of four groups of lesions, varying considerably in appearance and situated on the scalp, forehead, eyebrows, and nose, respectively. On the forehead, near the hair line, was a group of pigmented superficial varioliform scars, on which the diagnosis of acne varioliformis was mainly based. On the frontal region of the scalp there was an area about 3 inches in diameter, consisting of small, rough, pinhead-sized papular lesions. Near the left eyebrow there was a group of crusted lesions suggesting herpes zoster. On the right side of the nose was a group of pinhead-sized dull, reddish, firm, smooth nodules, suggesting syphilis, a tuberculid or iodism.

DISCUSSION

Dr. Highman said that the case interested him very much, though, except for the lesions on the forehead, it did not seem to him to be acne varioliformis. The group of fresh lesions on the nose strongly suggested a disseminated lupus vulgaris.

Dr. Williams said the case impressed him as acne varioliformis; the scars were typical and the chronic course sustained that diagnosis. As a rule, lupus vulgaris showed more general swelling, and would hardly present such distinct lesions and such small scars separated by normal skin. The scars were also very thin and soft, and there was none of the thickening one would expect in a disseminated lupus condition of the skin.

Dr. Howard Fox agreed with Dr. Highman that the lesions on the nose did not look like acne varioliformis, though the pitted scars on the forehead were perfectly typical of that disease. It was on account of the multiformity of the lesions that the case was presented.

GENERALIZED PRURITUS AND PIGMENTATION WITH HYPOADRENALISM. Presented by Dr. Levin.

B. P., a woman, 26 years of age, was born in Russia and had suffered from an intense pruritus for four years. Seven years ago the skin began to darken. She also complained of severe headaches, mental and emotional depression, and of fatigue. She had lost 30 pounds in seven years. Her urine was said to have contained sugar at one time, but she stated that she was then pregnant. She was married four years ago, had two healthy children, and had a miscarriage one year before. She was pregnant when presented. The menses were irregular, and painful, and the flow profuse.

The skin showed a generalized pigmentation and dryness. The increased pigmentation was most marked on the trunk. On the chest there were numerous areas of achromia which developed after scratch marks. The hair was dry. The nails were convex, dry, and showed pinpoint white spots and the presence of white crescents bordered distally by crescents of brownish-red color. Sergent's line was also present.

The patient's eye-slits were narrow and the pupils contracted, and increased lacrimation and salivation were present. The gag reflex was absent. The mouth temperature was 97.6 F. The blood pressure was: systolic, 96; diastolic, 64. The urine was negative for sugar, and no sugar was found in the urine after the ingestion of 100 gm. of glucose. The blood sugar was 0.1 and carbon dioxid 40.

GENERALIZED PRURITUS, PIGMENTATION, AND ECZEMA IN A PATIENT WITH ADRENALISM. Presented by Dr. Levin.

Y. Z., a woman born in Russia, aged 38, has been in this country for nine years. She had measles and typhoid fever in childhood and was operated on for an abdominal condition twelve years ago. Six months ago she was treated for tenia saginata, the diagnosis being confirmed by finding the ova in the stools. The menses began at 13, were always irregular, scanty, and accompanied by little or no pain. She was married fifteen years ago and had had five children, two of whom died from accidents. For the past six years she had suffered from pruritus which became very intense two years ago. She also complained of hyperidrosis of the flexor surfaces which appeared two years ago. She had had a recurrent evanescent eruption for six months, and patches of erythema with oozing for five months. For the past four months she had been having attacks of flushes followed by excessive perspiration. For two years she had been losing weight and strength and tiring easily; she had almost constant frontal headaches, a capricious appetite and marked constipation. She urinated every hour and had a loss of sexual desire.

The skin was dry, thickened, pigmented, roughened, and covered with follicular papules. The brownish pigmentation was marked on the trunk and was darkest along the axillary folds, the nipples, and the waist line. It was least noticeable on the lower extremities. There were patches of scaly, dark red, lichenified lesions on the face, the back of the neck, the upper extremities, and along the waist line. The hair was black, dry, coarse and thin, especially in the axillary and pubic regions. Sergent's line was present, and the hands were moist and cold. The eye-slits were unequal, the right being wider. The pulse rate was 72, and Aschner's sign was present. There was a systolic murmur at the apex which was not transmitted. The blood pressure was: systolic, 108; diastolic, 70.

Examination of the stools and urine gave negative results. Blood Chemistry: sugar, 0.08; carbon dioxid, 34; urea nitrogen, 0.15; nonprotein nitrogen, 0.28; red blood cells, 4,800,000; white bloodcells, 10,000; polyneutrophils, 64 per cent.; mononuclears, 35 per cent.; eosinophils, 1 per cent.; hemoglobin, 70 per cent.

ARSENICAL PIGMENTATION. Presented by Dr. Parounagian.

Mrs. D., had had one positive Wassermann reaction and had received one dose of neo-arsphenamin in the wards at Bellevue Hospital. Several weeks later she began treatment in the outpatient clinic. Following the third dose of neo-arsphenamin (0.54) she developed an exfoliative dermatitis on January 20, and when presented showed a pigmentation following the arsphenamin administration.

PIGMENTATION FOLLOWING ARSPHENAMIN. Presented by Dr. Parounagian.

Cornelia M., aged 24 and married, an Italian, had had four children, two of whom were living; one child had been born dead, the other died of pneumonia. Her father and mother were living and well. The rest of the family history was negative; the patient's previous history was also negative. Ten years ago she had a rash. When she first came to the Bellevue Clinic on Jan. 24, 1920, she presented a large mass in the upper quadrant of the abdomen. She was given three arsphenamin and two mercury injections, the third injection being given on Feb. 9, 1920. The next day she noticed a generalized itching and an eruption with marked pigmentation which remained until February 27. Neo-arsphenamin was used (m) 0.45 at each injection. On January 20, the Wassermann reaction was + + + +; on February 24, + + +. B. of H.

DISCUSSION

Dr. Williams recalled seeing one of the patients who had a well marked and interesting case. She presented on the upper part of the neck a typical pigmentary syphilid, but there was also, all over the anterior surface of the trunk, a pigmentation which in appearance was identical with that on the neck. Pigmentation on the neck is a well-known symptom of syphilis; that on the body is said to be due to arsenic: Was it not possible that these two manifestations were due to the action of the syphilitic poison and of arsenic, respectively, on the suprarenal glands?

Dr. Wise said that Dr. Williams' remarks led him to inquire whether these were arsenical melanoses, or pigmentation following arsphenamin injections. He did not know whether one could have a true arsenical pigmentation following arsphenamin. Was it a deposit of pigment from a previous dermatitis in a patient known to have had a skin eruption, or was it a true arsenical pigmentation?

Dr. Levin said that no matter what the etiology might be the same factors were active in producing the pigmentation. Whether the poison be a mineral or some other exogenous or an endogenous toxin, the pigmentation results from the presence of melanophores which are called forth to destroy the toxin and improve the oxygenation of the tissues.

LUPUS ERYTHEMATOSUS. Presented by Dr. Levin.

Mrs. B. S., aged 28, a native of Russia, was first seen about five weeks before presentation, when she applied for treatment of a scaly, pea-sized erythematous patch on the lobe of the left ear. It had been present for four months and had received no treatment. Under the application of astringent and soothing lotions and pastes, the condition would appear to involute but would then recur and slowly spread. The lesions presented on the cheeks appeared two weeks ago. The patient was a healthy person who exhibited a lesion on the lower third of the lobe of the left ear, an eruption dark-red in color, covered with fine adherent scales and showing beginning atrophy. On each cheek were two dark red, elevated tubercles, with scaling.

DISCUSSION

Dr. Highman agreed with the diagnosis.

Dr. Williams said that the patches on the cheeks at first thought suggested typical lupus erythematosus, but closer examination made that diagnosis seem doubtful. He did not believe that condition would produce such deep firm nodules as existed on the woman's cheeks—nodules of at least twice the diameter of the visible lesions.

Dr. Wise spoke of the resemblance of sarcoid to nodular lupus erythematosus in some instances and the association of the two conditions, and thought it quite possible that a microscopic section of one of the nodules on the right cheek might present the appearances seen in the sarcoid of Boeck.

Dr. Fraser hoped that Dr. Levin would settle the question of the diagnosis before the next meeting by injecting some of the material into a laboratory animal and by making an histologic section.

Dr. MacKee was inclined to regard the case as one of lupus erythematosus. The evolution of the lesion was rather rapid for sarcoid and, furthermore, the nodule gave the impression of being due largely to edema. Lupus erythematosus occasionally developed suddenly with the formation of edematous nodules. The speaker suggested this type of lupus as a tentative diagnosis.

LUPUS ERYTHEMATOSUS AND LICHEN SCROFULOSORUM OCCURRING IN A TUBERCULOUS SUBJECT. Presented by Dr. Mellon for Dr. Thorne.

Mrs. M. S., from Dr. Whitehouse's service at the Skin and Cancer Hospital, an Italian, aged 45, applied to the Outpatient Department for treatment, Dec. 23, 1919. At that time both cheeks and nose showed red scaly, slightly infiltrated lesions, and there were similar lesions on the margins of both ears. The redness did not disappear on pressure; there was no ulceration and no apple-jelly nodules. On removal, the scales showed keratotic spines which penetrated the ducts of the sebaceous glands. The condition had been present for about a year. The shoulders—especially the left—and elbows showed small, light-yellowish, lichenoid papules, some with slightly depressed centers and slightly scaly. This condition had been present six months. The physical examination showed an old tuberculous process in the left lung. The histologic examination of a papule from the shoulder showed: "In the upper part of derma are shown small scattered lesions 0.5 mm. in size, which are composed of closely packed endothelial cells, plasma cells, small mononuclears and a few polymorphonuclears; there were a few giant cells found in examining several sections. The epidermis overlying the lesion is thinned or entirely destroyed, i. e., there is ulceration. Ziehl's stain for acid fast bacilli, negative." The seeming ulceration of lesions on the face was probably due to local treatment—eight applications of a mixture of lactic acid, 4 parts, and phenol, 1 part,

DISCUSSION

The consensus of opinion seemed to be that it was a case of lupus vulgaris. having been made.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, April 6, 1920

JOHN E. LANE, M.D., *Chairman*

DYSTROPHY OF THE NAILS. Presented by DR. WISE.

A Greek, from Dr. Fordyce's clinic, aged 22, stated that the condition had existed for eight years. All the nails from the fingers and toes were almost obliterated. The patient stated that the condition began with the left thumb nail and spread rapidly to the others, including the toe nails. Examination for tinea was negative.

COLLOID MILIUM. Presented by DR. TRIMBLE.

The patient had been presented twice before. Microscopic examination had proved the condition to be one of colloid degeneration. Six radium exposures had been made, some of them lasting for an hour, with no benefit whatever. Formerly there were two or three lesions on the right side of the nose which were curetted and cauterized with good result.

CASE FOR DIAGNOSIS. Presented by DR. SCHEER.

The patient, Arthur L., aged 7, was from Dr. Fordyce's service at the Vanderbilt clinic. There was a history of a similar outbreak ten months ago, which lasted four weeks, and a second attack four months ago, which lasted ten weeks. The present outbreak had lasted one week. All outbreaks occurred in the same location, i. e., on the buttocks and extensor surfaces of both elbows. The lesions consisted of isolated and confluent bright red papules, varying in size from that of a pinhead to that of a split pea. The lesions did not disappear on pressure (hemorrhagic); some of them, especially the larger ones, had what looked like a central puncture. The mother stated that there was no itching or scratching. The child suffered from enuresis. He had taken no drugs except rhubarb and soda. Erythema multiforme was the most probable diagnosis.

DISCUSSION

Dr. Parounagian favored a diagnosis of erythema multiforme.

Dr. Trimble agreed with the diagnosis of erythema of a papular variety with hemorrhage.

Dr. Levin said that this type of erythematous, papular eruption is seen in children who have frequent attacks of bronchitis and tonsillitis and are subject to prurigo. The patient had a history of tonsillitis, bronchitis and nocturnal enuresis, and showed only one testicle in the scrotum and an epigastric hernia. The case suggested some form of prurigo, and the patient would be benefited by small doses of the pituitary gland.

DERMATITIS PAPILLARIS CAPILLITII. Presented by Dr. L. Chargin.

A man, white, aged 22, a chauffeur, had had the affection for two years. The condition began with the appearance of several small papules which gradually increased in number and size, and at the time of presentation covered the entire width of the upper neck at the hair border. There was no keloid formation.

VERRUCAE PLANAE. Presented by Dr. Max Scheer.

D. M., a man aged 32 years, from the service of Dr. Fordyce, Vanderbilt clinic, born in the United States, and with no occupation, presented juvenile warts (verrucae planae) on the left side of the chin and neck. The first lesions appeared nine months before, and they attained their present number in one month, remaining unchanged until the time of presentation. The lesions were numerous and ranged in size from that of a pinhead to that of a split pea. They were identical with the flat warts so commonly seen in the young. The hands were not affected.

SYPHILITIC SERPIGINOUS ULCERATION OF HARD PALATE. Presented by Drs. L. Chargin and E. Abramowitz.

Joseph G., aged 30, contracted a chancre ten years ago, and received one injection of arsphenamin but no further treatment. The present lesion in the mouth began four months before presentation, and consisted of a superficial moth-eaten-like ulceration, involving the gingival border and adjacent area of hard palate, and was arranged in a serpiginous manner. The Wassermann reaction was ++++. The condition had improved under one injection of arsphenamin and two of mercury.

ROUND ATROPHY FROM SYPHILIS. Presented by Dr. Levin.

M. Z., a man, a Russian by birth, was first treated at the Beth Israel Clinic six months before. He had a generalized eruption twenty-eight years ago, which was followed by the atrophic spots presented. Scattered over the trunk and extremities were numerous pea-sized to nickel-sized round, oval, and irregular depressed and level white atrophic spots. The Wassermann reaction was ++. Recently he had received eleven arsphenamin injections. Twenty-eight years ago he received twenty mercury inunctions and about a dozen injections.

DISCUSSION

Dr. Scheer suggested that a better name would be macular atrophy.

Dr. Highman said he did not understand the title of primary atrophy. He had never seen a case of primary atrophy with the majority of the lesions showing scar tissue. When a syphilitic ulceration heals, it usually leaves an atrophic scar, or a light hypertrophied scar (keloid) or one level with the skin. All these first types of cicatrization were present. Primary atrophy leaves a spot in which it is possible, on palpation, to get a sensation of entering a hernial ring; and in this instance he had failed in any of twenty scars or lesions to elicit that phenomenon. On the contrary, in some of the scars he could feel no depression whatever; other scars were flush with the skin, and in others there was hypertrophied scar tissue; so that the case did not seem to be one of primary atrophy, but simply presented the three different types of scars following syphilitic ulceration. Primary atrophy can be recognized without doubt under the microscope, and the accuracy of Dr. Levin's conception must be decided in that way.

Dr. Pollitzer said that the case impressed him as an atrophy and not as a scar. The normal fields of the skin were preserved over the lesions. He had examined only a few of the larger lesions and glanced over the rest without palpating or examining them closely, but felt convinced that it was really a case of atrophy. Dr. Levin would be able to correct him if he was mistaken in believing that the normal fields of the epidermis were preserved in all the lesions—the minute cuticular lines and even the indentations of the follicles.

Dr. Levin said he had been observing the patient for six months and was positive that there had never been any ulcerations. The man volunteered the information that these white atrophic scars appeared after the secondary papular eruption. This was the fourth case of the kind he had seen and all showed similar lesions. He would excise one of the lesions and let Dr. Highman examine it. In his opinion, the atrophy depended on the degeneration of the elastic fibers of the corium.

ANGIO-KERATOMA OF SCROTUM. Presented by Dr. Wise.

John L., aged 40, from Dr. Fordyce's service, was a native of France and a clerk. He presented on his scrotum a dozen pinhead sized, bluish-gray, soft tumors, isolated and not painful. They bled profusely when injured. He came to the clinic for scabies and did not know how long his scrotal eruption had been present.

DISCUSSION

Dr. Pollitzer said that clinically the case did not present keratosis. He thought it was simply a case of so-called angioma—a telangiectasis affecting the scrotum, like the "ruby spots" seen on the trunk and extremities in old people.

ERUPTION AFTER ARSPHENAMIN INJECTION. Presented by Dr. Levin.

M. F., a man, aged 47, was born in Ireland. Thirty years ago he had primary and secondary lesions of syphilis; at that time he received treatment of mercury by mouth for two years. During the past three years he has received twenty intravenous injections of arsphenamin. After the last five injections a general erythematous eruption appeared, which gradually faded and disappeared after ten days. A week ago he received an injection of arsphenamin (0.4 gm.), and four hours later developed a general intensely itchy eruption, made up of bean-sized to quarter of a dollar-sized round, dark red macules. These gradually faded, leaving several patches which are dark red in color and scaly.

DISCUSSION

Dr. Highman said that the case was a curious example of what Homer Swift designates as an anaphylactoid reaction. He himself had never seen it until recently when a patient at Mount Sinai presented the lesions shown in Dr. Levin's patient. They appeared on the legs, and a few of them were twice the size of those in Dr. Levin's case. The patient also had varicose veins, but the lesions were above as well as below these. He had been at a loss to explain the condition, but the two cases were so similar in behavior and appearance that possibly a group of conditions will be observed determining a distinct classification of a type of arsphenamin reaction, or one favored by the influence of arsphenamin on the body.

Dr. Pollitzer said he had a case under observation which he had treated for several years. In the beginning the patient was treated rather energetically and had no cutaneous reaction until after he had received treatment for more than a year in courses of three injections in three days. But during the second year of treatment he developed these patchy erythematous lesions, and later became so sensitive to the arsphenamin that on the last few occasions the rash appeared while the injection was in progress. First it appeared on the lower lip and chin, the skin becoming edematous and red; then similar red edematous patches appeared elsewhere on the trunk and extremities. The edema subsided, leaving a dusky erythema with desquamation and ultimate pigmentation, which lasted about three months and was uncomfortably pruritic. The eruption cannot be grouped with the arsenic eruptions; it was not like the desquamative dermatitis after arsphenamin used not wisely but too much. It seems to be due to sensitization, and in that respect differs from the ordinary drug eruption. It is not manifestly due to the elimination of arsenic from the skin, but to a vascular or neurovascular disturbance in the skin. This patient in the last two years has not received more than one injection in a course, for fear of the effect of persisting in the presence of this eruption. Dr. Pollitzer said that his first case of this kind was in a tabetic patient who is now dead. The rash appeared on the side of the neck a few hours after the injection, and as he had been playing golf the day before and the patches were not definitely circumscribed, the diagnosis of dermatitis venenata, made by the patient himself, seemed probable; but subsequent injections proved that it was not dermatitis venenata but was due to the arsphenamin.

Dr. MacKee said he had seen a dozen examples of immediate eruption resulting from injections of arsphenamin, and had had patients so sensitive that the eruption would appear during the early stages of the injection. Usually when it occurred during or within an hour after the injection, it had been urticarial in type; when it appeared the following day it was of the erythema multiforme type. In most of the cases in which it seemed advisable to continue the treatment, neo-arsphenamin was used, and the patients tolerated that very well.

Dr. Highman said that this case might be subjected to some interesting experiments. If the injections of arsphenamin were made at suitable intervals, one done as a control without previous preparation, three weeks later another given after an injection of suprarenal gland extract, and still later another after atropin, as suggested by Stokes, some valuable data concerning the mechanism of the process might be gained.

Dr. Pollitzer, referring to Dr. Highman's suggestions for experimentation with the case, said that he had preceded the arsphenamin injection with an injection of epinephrin and atropin at different times without visibly influencing the occurrence of the rash.

Dr. Abramowitz said that Dr. Pollitzer did well in calling attention to the fact that the eruption was not a purely arsenic dermatosis. Antipyrin and phenolphthalein were capable of producing a similar eruption. Dr. Chargin had presented a case before this section which was produced by arsphenamin. Previous administration of epinephrin or atropin, or both, did not act as a preventive.

Dr. Chargin said that in conjunction with Dr. Goldenberg he had presented a patient before the section (May, 1919), who had developed an eruption after the seventeenth injection of arsphenamin. Prior to the eighteenth injection he received a dose of epinephrin hypodermatically without preventing a recurrence, and at a later injection atropin was given, also without any effect in preventing eruption. The patient was subsequently given additional arsphenamin injections in another service, receiving epinephrin before and atropin after the injection; but despite that an eruption followed. Dr. Chargin thought that neither epinephrin nor atropin had any effect in prohibiting these eruptions.

Dr. Levin said that he had seen several anaphylactic reactions from the drug, but this was the most intense eruption of all. Atropin and epinephrin should prevent the attacks as well as diminish the intensity in these cases; but both must be given in large doses. The best effect should be obtained by combining both. The eruption seems to depend on a disturbance of the vegetative nervous system and probably a vagotonia. The epinephrin acts by stimulating the sympathetic and the atropin by inhibiting the vagus.

Dr. Levin would test this patient and present him again.

MYCOSIS FUNGOIDES. Presented by Dr. MacKee.

Philip N., aged 55, a Russian who had been in the United States twenty-four years, presented himself at Dr. Fordyce's clinic with an eruption on the trunk and extremities of five months' duration. The lesions consisted of raised, circumscribed dark red patches, the size of a dime and a twenty-five cent piece, showing follicular involvement. The patient complained of itching. He denied any previous eruption. The Wassermann reaction was doubtful; the blood count normal. The biopsy report showed the condition to be mycosis fungoides.

DISCUSSION

Dr. MacKee said that there were several interesting clinical features. First, there was no preceding fungoid eruption; second, the lesions developed as a group of follicular papules—like a small papular syphilid. When the patient was first examined and photographed, there were several lesions in different stages of development, one of them a group of follicular papules surrounded by erythema; a later stage showed infiltration together with the follicular element, and the latest stage showed a definite tumor. This was the only case the speaker had ever seen develop in this way.

Dr. **Pollitzer** said that if it had not been stated that the histologic picture was definitely that of mycosis fungoides, he would have guessed that it was a case of leukemia from the appearance of the lesions. A positive diagnosis, of course, could be made from the microscopic appearance, but clinically it did not appear to him like mycosis fungoides, nor did the history as given by Dr. MacKee suggest that diagnosis.

Dr. **Rosen** said that the case did not tonight present the interesting features shown four or five weeks ago when it was first seen. At that time the patient exhibited nodular, soft lesions raised above the skin a quarter inch, resembling the soft nodules of lupus vulgaris. These lesions had entirely disappeared under radium treatment, and the patient now presented lesions on the back that were rather new—macular papules with distinct scales. At first the diagnosis seemed to lie between leukemia cutis and mycosis fungoides, or possibly a bromid eruption.

Dr. **Trimble** said that in his opinion, based on a cursory examination, the case did not bear any resemblance to mycosis fungoides clinically. The report of the positive pathologic diagnosis was quite surprising, and since it was not always possible to say absolutely whether a case was or was not mycosis fungoides from a pathologic standpoint, he thought further confirmation was necessary. Clinically the case resembled some form of cutaneous sarcoma; the widely scattered, dark blue, infiltrated lesions suggested that diagnosis. He would like very much to hear a further report on the case at a later date. If it were eventually proved to be a case of mycosis fungoides, then it would have to be looked on as one with extremely atypical clinical features.

Dr. **Kingsbury** said that the case was interesting and unusual, and he would not know how to classify it clinically. It did not look to him like mycosis fungoides, nor could he see any resemblance to a leukemic state. It demanded more observation than the arbitrary accident of a microscopic diagnosis.

SYPHILIS IN ASSOCIATION WITH PITYRIASIS RUBRA PILARIS.

Presented by Drs. **Chargin** and **Abramowitz**.

Dr. **Chargin** said that S. W. was presented at the last meeting of the section, at which time a discussion arose as to whether the entire affection in the patient was syphilis, or whether we were dealing with a maculopapular syphilid in association with a pityriasis rubra pilaris—of both of which he seemed to show characteristic lesions.

The speaker said that there could be no doubt but that this patient showed typical syphilitic papules on his back when shown a month ago. They were pea-sized, shiny flat on top, bean colored, some with central depression and scaling; but in addition he showed follicular lesions scattered over the back, arms, neck and legs. Those on the back could easily fit into the picture of a follicular syphilis, except that they lacked the typical grouping. The lesions on the legs and hands fitted more closely into the picture of pityriasis rubra pilaris. The face showed a general infiltration in which individual papules could be made out, and which could readily be interpreted as a papular eruption "en nappe," and indeed this was the opinion of one of the discussers.

During the past month he had received five arsphenamin and six mercury injections with the result that the syphilitic eruption had entirely involuted, while the rest, although it showed some improvement, had for the most part remained. The speaker thought that it seemed to be clearly a case of syphilis in association with pityriasis rubra pilaris.

DISCUSSION

Dr. Abramowitz said that this was a particularly interesting case. It seemed to him that with the onset of the secondary stage of syphilis a coincidental eruption of what seemed to be a typical pityriasis rubra pilaris appeared. A section examined that afternoon conformed to that opinion. The eruption, especially on the face, had faded with four arsphenamin and five mercury salicylate injections. He believed there was no doubt of the association in this patient of pityriasis rubra pilaris and an early secondary syphilis.

Dr. Highman said that the case undoubtedly presented the two conditions as reported by Dr. Chargin, but that Dr. Abramowitz had evidently misunderstood his remarks concerning it. What the microscopic structure showed was merely an ordinary degree of hyperkeratosis with a dilatation of the blood vessels, which, however, were not increased in number. If there had been no hyperkeratosis and no dilated blood vessels, the tissue would have appeared normal. The picture was characteristic of nothing in particular, but was certainly not characteristic of syphilis.

Dr. MacKee expressed himself as still in doubt regarding the diagnosis in spite of having observed the case two or three times. The hands and forearms presented the picture of pityriasis rubra pilaris, but the follicular eruption on the body with the long spines resembled the so-called lichen spinulosus. Last month, the face presented a condition that one would not hesitate to call syphilis. The fact that the eruption on the face had disappeared suggested that the face eruption was syphilitic. In the speaker's experience syphilis "en nappe" did not disappear under vigorous antisyphilitic treatment as rapidly as did other syphilids.

Dr. Trimble said that the case undoubtedly bore a striking resemblance to pityriasis rubra pilaris. He wished, however, to direct attention to the fact that it also had some resemblance to Darier's disease (keratosis follicularis). The brownish granular condition around the temples covered with furfuraceous scales was a symptom seen in many cases of keratosis follicularis. The palmar keratosis would also fit in with such a diagnosis, though this latter symptom was also characteristic of pityriasis rubra pilaris. In nearly all cases of pityriasis rubra pilaris one or more large areas or plaques were usually observed; the case in question had no such large areas. The speaker said he was merely calling to mind a number of symptoms presented by this patient which would suggest keratosis follicularis; in all probability it was not that disease, as keratosis follicularis was comparatively easy to recognize pathologically; and since Dr. Highman had studied the slides it was not likely that he would have missed the so-called psorosperms.

Dr. Levin said that the patient showed over the left shoulder, arm and back, pea-sized to bean-sized lesions which had been formed by confluence of scaly papules and resembled lesions of psoriasis. Clinically the condition was pityriasis rubra pilaris in a syphilitic with dysfunction of the glands of internal secretion. The patient showed the female type of pubic hair, had long extremities with muscles which looked overstretched. A roentgenogram of the sella turcica might show a large pituitary gland in a sella with changes, and the chest might show a large thymus. In his opinion, the skin condition depended on a further disturbance of the glands of internal secretion by the syphilitic infection. He suggested the use of glands in conjunction with antisyphilitic therapy.

Dr. Chargin, referring to Dr. MacKee's remarks, said that if the entire affection were syphilitic in nature, one would have noted a more marked involution of the eruption in response to the treatment, as happened in lesions regarded as syphilitic. It should be borne in mind that pityriasis rubra pilaris is influenced by arsenic, and much of the improvement shown in the pityriasis signs must be attributed to that.

GUMMA AT SITE OF ORIGINAL CHANCRE. Presented by Dr. L. Chargin.

A man, aged 35, gave a syphilitic history dating back to 1913, when he had a chancre with marked induration followed in due course of time by a secondary eruption. In that year he had received five arsphenamin and four mercury injections, but no further treatment to date. Two weeks ago he returned with a typically punched out pea-sized ulcer at the site of the original chancre. The history was that it began with a deep seated nodule which ulcerated. The last coitus took place more than four months prior to the development of the sore. The site of the ulcer was quite indurated. There was no inguinal adenopathy; the dark field for spirochetes was negative, as was the Wassermann reaction.

BASAL CELL EPITHELIOMA. Presented by Dr. Abramowitz.

A young lady, aged 19, a native of the United States, who presented herself at Dr. Fordyce's clinic; had had the condition three years. There was a pea-sized, well defined lesion on the upper lip with a pearly border and depressed center. There was slight crusting and occasional bleeding. The case was interesting on account of the youth of the patient and the location of the lesion. The history was definite, and the lesion characteristic.

DISCUSSION

Dr. Wise said that the patient was presented as an unusually interesting example of basal cell epithelioma appearing at the age of 19. There was no doubt of the diagnosis, as the lesion was typical in every respect.

NODULAR SYPHILID. Presented by Dr. Wise.

A woman, aged 38, born in the United States, was under observation at the Vanderbilt clinic. The duration of the condition was two and a half years. There were several nodules on the nose which had ulcerated, the whole lesion being on an erythematous base. A year ago the Wassermann reaction was negative, and a week ago several Wassermann tests proved negative. Provocative treatment was being given, and the case would be reported again later.

The case was interesting on account of the duration—two and a half years—which would make the diagnosis of syphilid seem doubtful.

DISCUSSION

Dr. Pollitzer said the lesions were not characteristic of lupus vulgaris. The fact that the process began in a woman during the fourth decade of her life spoke against tuberculosis, although not absolutely. The negative Wassermann test also spoke to some extent against syphilis—but the diagnosis manifestly rested between a syphilitic and a tuberculous process. On the whole, he was inclined to think that it was a syphilitic condition. The important factor against tuberculosis was the age of the patient, as that disease rarely begins so late in life. A negative Wassermann reaction with a single lesion of that kind meant little. In his opinion the patient should receive antisyphilitic treatment. A biopsy, unless extensive and disfiguring, would probably show nothing definite, unless the bacillus was found, which in cases of this kind rarely happens.

Dr. Kingsbury agreed with Dr. Pollitzer in regard to advisability of antisyphilitic treatment, but was inclined to think it was a case of lupus vulgaris.

Dr. Parounagian agreed with Dr. Pollitzer, and expressed the hope that after the patient had received arsphenamin and mercury injections she would be presented at the next meeting.

Dr. Wise said that he should have stated in the history that the husband had active syphilis and was receiving treatment. The case would be reported in more detail at the next meeting.

Note: Further observation proved that the lesions were tuberculous.

LEUKODERMA SYPHILITICUM. Presented by Dr. Chargin.

A mulatto girl, aged 19, gave a history of a sore on the genitals one year prior to presentation. followed by secondary lesions. At that time she received a number (eight or ten) of arsphenamin injections and mercury by inunction. When first seen ten weeks ago, she presented a papular eruption and leukodermatous areas, the counterpart of the lesion shown at the time of presentation. Under intensive antisyphilitic treatment (six arsphenamin and ten mercury salicylate injections in a period of seven weeks) the eruption involuted, leaving round and oval pea to five cent piece sized leukodermatous areas. The involution of the papules took place from the periphery toward the center, thus producing the depigmented areas. At this time she was discharged from the hospital. During the past two weeks the eruption recurred at exactly the same locations as the eruption of ten weeks before, and of the same character. At the time of presentation she showed an extensive papular eruption varying in size from that of a pea to that of a five cent piece and occupying the former leukodermatous areas. Some of the depigmented areas showed no papulation. The affection covered practically the entire body. In many instances the papules did not cover the entire depigmented areas, thus leaving a leukodermatous collar surrounding a papule. Mucous membranes were negative. There were no subjective symptoms and the Wassermann reaction at this time was negative.

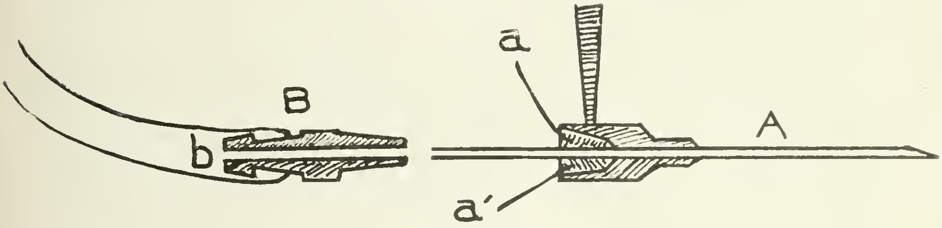
DISCUSSION

Dr. Chargin said that it is usually accepted that the leukoderma which occurs in the course of syphilis follows in the wake of a formerly existing eruption either macular or papular. In a considerable number of cases in which particular attention was paid to this question, that did not seem to be the case in the majority of patients. As a general rule, one usually sees a general pigmentation, especially of the neck and its adjacent area, in which in due time these round depigmented areas appear. The case presented was the first that he had seen in which a papular eruption was followed by a leukoderma.

Dr. Parounagian said that the race may have been responsible for the appearance of this case.

MODIFICATION OF THE FORDYCE NEEDLE. Presented by Dr. Abramowitz.

Dr. Abramowitz presented for inspection a modification of the Fordyce needle that could be used for making a Wassermann test. By attaching a Luer adapter, arsphenamin can be introduced through the same needle. With the introduction of the needle into the constricted vein, blood comes out in a tubular stream into a receptacle. When the tourniquet is released only a few drops of blood escape before the adapter is applied if arsphenamin is to be administered. The field of operation is therefore quite clean.



Modification of the Fordyce needle. *A,* cross section of the needle; 18 gage, actual size; *a a,* groove into which Luer adapter slides; *B,* Luer adapter; *b,* rubber tubing.

SCLERODERMA; BAND-LIKE. Presented by Dr. Rosen.

Mrs. M., aged 26, born in Russia, gave an indefinite family history. The condition exhibited began about six years before with a hardening of the skin above the knee, which later extended upward and downward. About three months after the lesions appeared, ulcerations occurred within the hardened skin area. These were treated with ointment and radium. The patient presented a band-like scleroderma extending along the entire length of the outer side of the left leg, with smaller isolated morphea-like lesions.

DISCUSSION

Dr. Rosen directed attention to the purplish hue of the band, with perhaps a thinning of the subcuticular fat, and asked whether it might be a beginning acrodermatitis—chronic atrophy.

Dr. Levin said he had some recollection of having seen this patient at the Post-Graduate Hospital, where she gave a history of having been treated for tuberculosis of the thigh. At that time she showed an irregular ulceration of the thigh with large scars and apple-jelly-like nodules. Dr. Whitehouse confirmed the diagnosis of tuberculosis.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, March 17, 1920

CLARENCE BAER, M.D., *president, in the chair*

A CASE FOR DIAGNOSIS. Presented by DR. MITCHELL

A man, aged 41, presented a reteform telangiectasia, which had been present for two years, associated with marked dermographism. The telangiectasia was limited to the trunk and arms. The disorder came on gradually, and had remained stationary. There were no subjective sensations.

DISCUSSION

DR. WILE was impressed with the similarity of the condition to a roentgen-ray telangiectasia. Then he said that it might be an unusual form of urticaria pigmentosa. There were marked wheals, and considerable pigmentation. He found it hard to accept the case as angioma serpiginosum as described by Hutchinson and thought it belonged to an entirely different group. He could not satisfy himself that the section showed any marked degree of venous congestion under the microscope. He had no diagnosis to offer.

DR. COLE thought the condition was either angioma serpiginosum or urticaria pigmentosa. He was more inclined to the former diagnosis.

DR. MITCHELL called attention to the fact that there was a marked dermographism, and that the lesions were limited largely to the upper extremities and the trunk. The appearance of the lesions led him to believe that the disorder was probably angioma serpiginosum, but he was not sure that this was the correct diagnosis.

FOLLICULITIS WITH MARKED SCARRING OF THE SCALP. Presented by DR. MITCHELL.

A man, aged 30, had a scalp disorder of fourteen months' duration. When first seen there was a severe folliculitis of the scalp. The Wassermann reaction was positive and the patient was under treatment. The use of salicylic acid and sulphur ointment had greatly improved the folliculitis.

This man was exhibited for comparison with the patient shown at the January meeting with the convoluted lesions in the scalp.

DISCUSSION

DR. WILE recalled the fact that at the January meeting there was a discussion as to what cutis verticis gyrata was, and also as to the nature of folliculitis decalvans. He thought this case illustrated admirably how those two conditions could be confused in the same patient. The man had definite areas of alopecia following lesions which were undoubtedly folliculitis decalvans, and also had a condition on the back of the neck which was cutis verticis gyrata.

DR. COLE did not agree with Dr. Wile. He thought the whole picture could be put down as dermatitis papillaris capillitii, with scar formation which was limited to the base of the neck.

Dr. Quinn said the lesions on the back were sebaceous and asked whether any of them had been opened.

Dr. Baer agreed with Dr. Wile.

Dr. Mitchell said that when the patient was first seen he had marked pustulation, which had all cleared up. The case had been interesting to him on account of the discussion regarding cutis verticis gyrata, the patient shown in January and this man bore only a superficial resemblance to that disorder. The skin in these two cases did not have the feeling of the skin of a dog's back, and could not be lifted up. In cutis verticis gyrata the ridges are devoid of hair and the whole skin can be easily moved on the scalp, which was not true of either the patient seen in January or this patient. He thought the present case could be described as a severe folliculitis with a slight tendency to keloid. The long ridge at the occipital region was not a scar; there were scars on the vertex but no hypertrophy.

CASE FOR DIAGNOSIS. Presented by Dr. Mitchell.

A man, aged 32, had a lesion in the palm of the right hand, with an apparent fibrous ankylosis, due probably in great part to holding the hand in partial flexion to avoid the production of fissures. The lesion had been present for a year and had remained stationary. Apparently the patient had had dermatitis on the dorsal surface of both hands before the present lesion developed.

The lesion occupied the entire palmar surface and extended to the proximal phalanges. It was well defined, erythematous, indurated, keratotic and, in places, fissured. The fingers could not be completely extended either actively or passively.

DISCUSSION

Dr. Cole said that the lesion was so sharply defined along the border that even if the Wassermann reaction was negative he would use antisyphilitic treatment.

Dr. Quinn said the condition was unusual. The man's hand was crippled as if it had been held in the same position for a year or two, and he stated that it came from a single lesion which had gradually enlarged. He thought antisyphilitic treatment was justified.

Dr. Eisenstaedt thought the patient would have to be kept under observation for some time. The peculiar, sharp demarcation first suggested a parasitic involvement, although it was rather marked for a parasitic condition. He thought the reason the hand was held in one position was that it pained to extend it.

Dr. Baer thought the man's ankylosis was purely functional. In spite of the fact that he had been doing the same office work for seventeen years, he believed it might have had something to do with his occupation.

Dr. Mitchell said he had seen a few cases which suggested this case. The patient was seen that day for the first time. There was no history of syphilis and the Wassermann reaction was negative, but the patient had immediately been placed on antisyphilitic treatment. Until it was demonstrated that the condition was not syphilitic, he would have to withhold a diagnosis. The patient would receive intensive treatment, and a later report would be made regarding the result.

URTICARIA PIGMENTOSA. Presented by Dr. Oliver.

A woman, aged 38, had an eruption which had been present for four years. It became worse when she was excited and at times typical wheals developed. The majority of the lesions were situated on the back, arms and chest. When she was nervous or excited, intense itching was present.

DISCUSSION

Dr. Mitchell said the question of urticaria pigmentosa would have to be considered. The adult cases he had observed, three in all, were somewhat different. The lesions were brown, rather than bluish-red, as in this case, and the lesions in those cases were somewhat better defined. There was urtication, but he could not determine whether it was limited solely to the lesion or not.

Dr. Oliver thought the case was one of urticaria pigmentosa. He had seen the patient twice. The history of definite wheal formation and the general appearance of the eruption at times led him to make the diagnosis of urticaria pigmentosa. A biopsy had been made and he would report the results later.

A CASE FOR DIAGNOSIS. Presented by Dr. Waugh.

A man, aged 45, had numerous subcutaneous tumors on both forearms and a few above the elbows. The disorder had been present for twenty years. The tumors varied in size from that of a hazelnut to that of a small hen's egg; they were rather firm, more so than usually found in lipoma, not painful, and the overlying skin was not discolored. There were many pinhead-sized scars on both forearms. The tumors were not in the usual location of enlarged glands and the lymphatics elsewhere showed no changes. No similar lesions were present on the body or lower extremities.

DISCUSSION

Dr. Wile thought it was impossible to say anything more about the case than that it was probably one of benign subcutaneous tumors. In all probability the tumors were neurofibroma, but it was absolutely impossible to diagnose them without a microscopic examination. They might well be neuroma, but most tumors of this kind are neurofibroma.

A CASE FOR DIAGNOSIS. Presented by Dr. Mitchell.

A man, aged 20, had a lesion on the right pillar, which had been present for one week. The Wassermann reaction was negative, as was also the examination for spirochetes. Little soreness was present. The patient had been sent in to be examined for syphilis. The last exposure occurred in January.

DISCUSSION

Dr. Cole thought it was a primary lesion of the tonsil.

Dr. Quinn believed it was a primary lesion, but the fact that the organisms had not been found under the microscope meant that the patient would have to be kept under observation for some time. He thought a diagnosis should be made positive before treatment was instituted.

Dr. Mitchell called attention to the fact that there was marked induration and that there was much difficulty in finding the organism in the mouth. He got three good preparations with no spirochetes in them. He could not puncture the lesion or use a Wright pipet, and it was difficult to get material. There had not been time for the development of regional adenopathy. He assumed that it was a chancre and the patient would be given intensive treatment on this assumption.

Dr. Stillians thought it was wrong to give antisyphilitic treatment without a definite diagnosis and thought the man would be better off if they waited a few days. He would rather have syphilis than syphilophobia, and be under the shadow of having the disease when it did not exist.

Dr. Cole said that one of the best schools in the country advocated going ahead and treating such patients, but he felt that one would not be justified in giving treatment until a diagnosis was made.

Dr. Mitchell said that if the lesion were on the finger or the genitalia where it could be easily reached and punctured carefully without dilution by the saliva, diagnosis would be a simple matter. So far as he knew, he had never been unable to find the organism when a chancre was present. In this case the lesion was not on the tonsil but on the pillar; it had all the appearances of a chancre, and there was no soreness. If it was not a chancre, what was it?

Dr. Stillians believed a diagnosis of chancre could not be made from the clinical observation alone and that a diagnosis could not be made until other signs were present. He said care should be taken about starting a patient on treatment before a diagnosis had been made. He once had a canker sore on his tongue that was treated with silver nitrate and remained for a month. He showed it to the students as typical of chancre in appearance.

Dr. Lieberthal said that he would institute treatment without delay when life or important function was threatened by a suspicious lesion, even though the laboratory findings were negative. In this case he thought it would be more advisable to delay treatment.

Dr. Baer agreed with Dr. Mitchell that the patient should be treated vigorously, in spite of the fact that no spirochetes had been found.

PSORIASIS. Presented by Dr. Senear.

A child, aged 7 months, had been brought in with a diagnosis of napkin dermatitis. The condition began two months previously and had spread rapidly. Fungus examination was negative. The child had been seen but once, and since the last visit lesions had appeared on the side of the neck.

DISCUSSION

Dr. Wile suggested the diagnosis of psoriasis.

Dr. Cole thought it was a seborrheic eczema, which would probably develop into psoriasis.

Dr. Mitchell thought the diagnosis lay between seborrheic dermatitis and psoriasis. The child was very young to have psoriasis, but it might be that disorder.

Dr. Eisenstaedt said that cases of psoriasis had been reported at 6 weeks, and he had seen one case at 9 months. He thought that the lesions below the knee were typical of psoriasis.

Dr. Senear said that when he first saw the child the lesions were not nearly so profuse as they were at present. He had thought it was a fungus infection, with secondary dermatitis around the genital region, due in large part to the napkin or urine. The next time he saw the baby the lesions on the neck had developed and he now believed it was a case of psoriasis. The lesions were more elevated, the scales were developing the silver color and had the distribution of the psoriatic scale. Examination for fungus had been negative and there was little greasiness of the scales.

ERUPTION ON LEGS. Presented by Dr. Oliver.

A girl, aged 2½ years, had an eruption on both tibial surfaces, which had appeared four months previously, one month after a severe attack of "stomach trouble." The disorder began as a clear spot which became indurated at the periphery as it spread. There were several spots on the tibial surfaces and one on the back. No subjective sensations were present.

DISCUSSION

Dr. Wile thought the case was unique. It was hard to get any idea from the lesions on the tibia as to exactly what the condition was. The lesions felt firm and hard and impressed one at first glance as the type of lesion found in erythema induratum or erythema nodosum, but they were painless and had a more doughy consistency than those lesions. On the back the lesion had the violaceous margin of a lesion which had undergone complete involution, and he believed the case was one of localized scleroderma.

Dr. Mackey suggested the diagnosis of erythema annulare.

Dr. Cole agreed with Dr. Mackey. There was a history of a contusion a few days ago, and he thought the bluish color on the back was due to the contusion.

Dr. Oliver said that there was no lesion in the lumbosacral region a week previously, but the mother told him the child had fallen against a chair a few days before. The only lesion present besides those on the legs was one in the center of the back. The lesion on the right tibia had enlarged and had a harder rim than when first seen a year ago. He thought it was a case of granuloma annulare and he would try to get a section and report later.

Dr. Baer believed it was a case of localized scleroderma.

SARCOID. Presented by Dr. Finnerud for Dr. Ormsby.

A woman, aged 24, who had been shown on several former occasions, was exhibited at this time with a histologic section showing characteristic sarcoid.

DISCUSSION

Dr. Eisenstaedt thought the lesions on the fingers were apparently an integral part of the condition, and while the cases of sarcoid were being divided into various groups, the case looked to him like tuberculosis on account of the finger lesions. He would feel much disappointed if tubercle bacilli were not found.

Dr. Finnerud said they thought the micro-organisms were there and they were making every effort to find them, but so far they had not been able to demonstrate any. A further report would be made later.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by Dr. Stillians.

A Jewish tailor, aged 52, who presented a lesion in the groin and anal region, in 1919 had had enlarged glands removed from the inguinal region. On presentation an ulcer about 3 cm. in diameter was seen in the furrow just posterior to the anus. Papillary projections which bled on slight provocation filled the ulcer. Large, separable, nontender glands were palpable in both axillary and inguinal regions and in the left posterior cervical triangle. Evidence of fibroid phthisis had been found in the patient's chest.

DISCUSSION

Dr. Eisenstaedt thought it was not tuberculosis verrucosa cutis, but tuberculosis vera cutis, or tuberculosis propia cutis.

Dr. Senear did not think it was a verrucous lesion in any sense of the word, and suggested a diagnosis of tuberculosis cutis orificialis.

Dr. Stillians thought the suggestions were very good. He had not been able to demonstrate anything in the pathology, but believed the man had tuberculosis. The glands that had been removed were probably tuberculous and he would make a further investigation.

LUPUS ERYTHEMATOSUS. Presented by Dr. Stillians.

A German woman, aged 70, had always been well until one year ago when an eruption appeared on the forehead and rapidly increased. On the forehead were four small patches from 1 to 1.5 cm. in diameter, bright red and partly covered by large, adherent scales. Over both cheeks, extending down over the angle of the jaw, were similar patches with central scars. Small patches were present on the ears.

DISCUSSION

Dr. Stillians believed the case was one of lupus erythematosus, developing at the age 69. It had spread so rapidly and had such a brilliant color that it seemed to him rather unusual. Most of the cases he had seen in old people had been lupus vulgaris erythematoides, but this was different.

ERUPTION ON SCALP. Presented by Dr. Stillians.

A man, aged 33, an American, a mechanical engineer by occupation, had had an itching eruption in the scalp for the past five years, which got better and worse. Loss of hair began in 1917; there was considerable baldness at the vertex and on the sides in the frontal region. Scattered over the scalp were superficial pustules 2 to 3 mm. in diameter, some of them springing from apparently normal skin, others having an inflammatory base. Many of them had ruptured and a blood crust had resulted. There were few scars on the scalp and none on the forehead.

DISCUSSION

Dr. Stillians said that Dr. Pusey maintained that the crusts found in pityriasis were due to scratching. This patient had an itching of the scalp with loss of hair and pustules appeared in considerable numbers at times. He could not find scars enough to make a diagnosis of acne varioliformis and believed the pustules were part of the picture.

ACUTE PSORIASIS. Presented by DR. STILLIANS.

A man, aged 25, had had psoriasis several years ago which had cleared up. Following an attack of influenza several weeks before spots had appeared on the forearms, legs, and scattered over the body. The eruption consisted of small papules with a slight amount of scaling. On the face was a profuse eruption, dull, brownish-red in color, also with slight scaling, in patches forming a reticular network.

DISCUSSION

DR. QUINN thought it was a case of psoriasis, with possibly some seborrheic element present. He suggested treating the face with sulphur ointment and thought chrysarobin should not be used at this time.

DR. SENEAR agreed with Dr. Quinn. The patient presented the small type of lesions often seen in psoriatic cases that were borderline cases between psoriasis and seborrheic dermatitis.

DR. STILLIANS said he showed the patient because he had not seen many cases in such an early stage and because of the marked involvement of the face. He asked for further suggestions as to treatment.

DR. SENEAR thought the tendency of arsenic, when used in the early stages, was to bring out the eruption severely. He recalled a case seen with Dr. Wile in which a man had just begun to develop the disease and was given rather large injections of arsenic by his physician. Within two days he was completely covered with an eruption such as this man presented. This was not true in the later stages, of course, but he believed the patient would be harmed by arsenic at the present stage of the disease.

DR. LIEBERTHAL said that in his experience, when a generalized eruption occurred, arsenic worked like a charm. As this case had developed so acutely, he believed autoserum would be of great benefit.

DR. MITCHELL said that every one ridiculed the autoserum treatment, but he and Dr. Frost had seen a case recently which demonstrated either the capriciousness of psoriasis or the efficacy of autoserum—perhaps both. They gave a patient from out of town five autoserum injections and recommended chrysarobin, but the patient never had to use it. When he presented himself at the end of five weeks he was entirely cleared of all lesions. In his experience Dr. Mitchell found the first injections of autoserum of much value; after that they were of less value, and sometimes of no value. He was inclined to agree with Dr. Senear in regard to the contraindication of the use of arsenic in the acute exacerbation of psoriasis.

DR. BAER said that several years ago he had four cases of psoriasis that, as far as he could see, were just about alike as regarded the conditions of the patients and the distributions of the lesions. He kept them under observation in a hospital and treated them with autoserum. They were given nothing but the injections; two cleared up nicely and the other two showed no effect.

BLASTOMYCOSIS IN A NEGRO. Presented by DR. ZEISLER.

A Pullman porter, aged 38, had an eruption on the neck which had been present for ten years. He had been treated at various times for syphilis, lupus and other conditions, with mercury and iodids. He had also received radiotherapy several years ago. He presented a verrucous patch with an elevated border, and in the minute abscesses blastomycetes were found. Under treatment with iodid for the past six weeks, radiotherapy and copper sulphate locally, there had been marked improvement.

DISCUSSION

Dr. Lieberthal thought that the true aspect of the lesion had been completely changed by the treatment the patient had received. The center of the lesion looked like a necrotic radiodermatitis; he, therefore, advised against the further use of the roentgen rays.

Dr. Quinn said he understood that blastomycetes had been found.

Dr. Cole thought it was a case of blastomycosis.

THE CHICAGO DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, April 14, 1920

William A. Quinn, M.D., *Presiding*

LESION OF THE RIGHT PALM. Presented by Dr. Mitchell.

This patient was the man with the palmar lesion who was shown at the March meeting. The Wassermann reaction had been negative, but the patient had received two intravenous injections of arsphenamin and some radiotherapy. A Wassermann test made on the day of presentation was again negative. Marked improvement was apparent, but there was still definite evidence of fibrous ankylosis.

DISCUSSION

Dr. Foerster had not seen the patient at the March meeting; at present the lesion was suggestive of a dermatitis factitia. There was sharp definition. with an appearance as if the lesion had been caused by some external irritant. He would not venture a diagnosis.

Dr. Waugh thought it was remarkable that the case had cleared up so extensively. He was interested to know whether the improvement was due to arsphenamin or radiotherapy.

Dr. Quinn considered the case most interesting and believed the condition of the hand was due to the severe pain produced when the man attempted to straighten it. The lesion was sharply defined, which Dr. Quinn thought was suggestive of syphilis. The case showed that one should not depend too much on a negative Wassermann reaction, and he believed the improvement was due to arsphenamin and not to radiotherapy.

Dr. Eisenstaedt asked how one would account for the severe constant pain if the case was one of uncomplicated syphilis.

Dr. Mitchell said that in spite of the negative Wassermann reaction the patient had received two injections of arsphenamin and also five roentgen-ray treatments. Marked improvement was manifest after the arsphenamin treatment. He did not believe it was a trade dermatitis, for there was nothing in the patient's work to lead one to that conclusion. The finger was still fixed in ankylosis and he could not straighten it, although the skin was considerably softened.

Dr. Mitchell stated that the patient with the lesion on the pillar, also shown at the March meeting, had returned twice for examination, but no spirochetes were found. The lesion was about the same at the time of his last visit, after which he disappeared from observation and he had not been heard from since.

A CASE FOR DIAGNOSIS. Presented by Dr. Eisenstaedt.

A girl, aged 20, presented scaling areas of the skin of one year's duration. She was first seen five or six weeks before presentation, at which time there were scaling areas on the sides of the chin and a circular lesion on the neck. Erythema was present on the neck but not on the chin. The menstrual history was irregular with much disturbance at this time. Naftalan ointment had been used on the scaling areas and the patient had been put on corpus luteum in 5 grain doses four times daily. Marked improvement was evident. Repeated examinations for fungi had proved negative.

DISCUSSION

Dr. Lieberthal thought it was a simple seborrheic patch and said that he had seen numerous cases of this kind.

Dr. Senear thought it was a case of seborrheic dermatitis.

Dr. Ormsby said that when he worked with Colcott Fox he was always calling attention to the early stage of seborrheic dermatitis as being what was ordinarily called "chaps." He had seen a great number of such patches on the face with little erythema and thought the lesion on the chin in this case was seborrheic dermatitis. The other lesion was either seborrheic dermatitis or a fungus infection. Dr. Eisenstaedt was well qualified to determine the latter condition and since he had said that no fungi had been found, the lesion was doubtless of the same nature as the other lesion on the chin.

Dr. Ormsby was not familiar with cutaneous lesions of this type produced by disturbance of the glands of internal secretion.

Dr. Eisenstaedt said he was glad to have the diagnosis made for him. He had placed the diagnosis of seborrheic dermatitis on the record, with a question mark. There was no eczematous character to the condition at any time and no greasiness of the scales. They were perfectly dry. He had given the patient a tube of lanolin and she had been taking large doses of corpus luteum for four weeks. The lesion on the chin had relapsed and the condition would probably have to be classified as seborrheic dermatitis, but it was not typical.

Regarding the glands of internal secretion dermatitis, some work was being done by the Swiss and Italians and Dr. Eisenstaedt thought that some of the findings in regard to malfunctioning of the endocrines would account for some of the hitherto unexplained dermatoses. He had once shown a girl of 23 who had not menstruated more than eighteen times in her life and who presented a typical dermatitis herpetiformis. Her condition afterward cleared up entirely on corpus luteum.

Dr. Quinn recalled a case of lupus erythematosus in a young man who was treated by the late Dr. Zeisler, who used carbon dioxid snow on a patch about the size of a silver dollar. This afterward progressed and Dr. Quinn was consulted. He used radiotherapy for some time, without effect. The patient went to Michigan where he remained for some time and saw a physician there who told him he did not know what the trouble was but he could clear up the condition, which he did by administering thyroid extract. The patient returned with the face clear.

Dr. Stillians thought that in dermatitis herpetiformis suggestion was an important factor. The patient whom he had shown at the February meeting with the exfoliative dermatitis was put on thyroid extract and had improved somewhat.

SCLERODERMA. Presented by Dr. Lieberthal.

A man, aged 62, had suffered from eczema of the right leg for five years. In January, 1920, he contracted a severe cold and the leg began to swell and became red. On the advice of a physician he used hot applications of boric acid solution, which produced a burn. The burned area healed by the end of February, but the leg remained hard and swollen. The rest of the skin was normal.

DISCUSSION

Dr. Ormsby thought the induration was similar to that in a case in which the circulation had been interfered with. He had seen a good many cases of severe dermatitis with as marked induration which was due entirely to hypertrophy from poor circulation. The small lesions on top of the skin looked like hypertrophic sebaceous glands, which could be produced in the same way.

Dr. Eisenstaedt said he had interpreted the small, whitish elevations somewhat differently from Dr. Ormsby, although he thought the exciting pathologic process was rather similar. He thought it was hypertrophy of the lymphatics rather than of the sebaceous glands.

Dr. Senear thought the underlying condition was scleroderma. He had been particularly impressed as the man walked out of the room. The lesions ran up the calf in a bandlike configuration. If the case was one of scleroderma the question of the hot applications was interesting, as it was known that trauma produced scleroderma in some cases. The verrucous lesions were circular and of sebaceous origin.

Dr. Mitchell said that he had seen cases in which a hard induration was present which was due in large part to disturbances of circulation. He had no opinion as to the verrucous lesions.

Dr. Lieberthal stated that the patient had an eczematous condition for four or five years and in January of this year contracted a severe cold. during which the leg became considerably swollen and reddened. His physician advised the application of hot boric acid solution and this was applied so hot that it injured the skin. Another doctor was consulted, who advised treatment for healing the burn—the burn healed in about six weeks, after which the leg took on the present appearance.

Dr. Lieberthal thought Dr. Ormsby's suggestion was a good one, but he could not reconcile himself to accepting the idea that the interrupted lymphatic circulation was able to produce such a hardening of the tissues in the space of six weeks. He thought the case could be interpreted in the beginning as one of trauma, added to a slight degree of scleroderma, and that the papillary lesions were the result of the burn. He would keep the patient under observation, try to secure a biopsy and present him again later.

Dr. Ormsby thought that if Dr. Lieberthal had not examined the patient just before the acute inflammatory condition appeared, he could not judge. Scleroderma rarely developed in that way; he had seen chronic eczemas that went on in that way for a long time. The edematous variety of scleroderma does not begin in a chronically inflamed area as a rule, but a chronic eczema of the leg could produce this picture readily, and he felt that this was the case.

Dr. Lieberthal thought if this was the case that some changes would be evident in the foot, but the foot was unchanged in any way.

Dr. Ormsby stated that he had said nothing about the lymphatics, but thought it was interference with the venous circulation that had produced the changes.

Dr. Eisenstaedt thought the question of the foot not being swollen was not vital, for the deep lymphatics might be unaffected even though the superficial ones were involved in the disturbance. The deep lymphatics might be draining very well.

ANGIONEUROTIC EDEMA. Presented by Dr. Eisenstaedt.

A colored man, aged 27, presented elevated patches on the shoulders and back and gave a history of their having appeared five days before presentation, following indulgence in shrimps.

DISCUSSION

Dr. Mitchell thought it was an angioneurotic disturbance of some kind.

Dr. Senear agreed.

Dr. Ormsby said he had been seeing quite a number of cases of rather severe intoxication due to the administration of influenza vaccine, and asked whether the others had had the same experience. The cases begin as urticaria and some patients develop a severe dermatitis following the injection of the vaccine. It would be interesting to know whether there was any such history in this case.

Dr. Eisenstaedt said that it was difficult to get a history in the case. In addition to the lesions on the body there was a dermatitis papillaris capillitii (Kaposi) on the back of the patient's head.

A CASE FOR DIAGNOSIS. Presented by Dr. Eisenstaedt.

A colored woman, aged 52, with multiple tumors of the breast and of the scalp, twenty-five years ago had a small elevated growth on the right breast near the nipple, which was removed surgically. Ten years ago she noticed a tumor of similar character on the same breast, but not in the line of incision. She then noticed a tumor on the left breast and these have been followed by others on both breasts, lower abdomen and right side.

The tumors were reddish-brown, elevated, infiltrated and of various sizes up to 7 cm. in diameter. The initial lesions were round, dark brown, elevated and hard and seemed to spread peripherally, with central scarring. The Wassermann reaction was negative. Blood examination showed a normal picture, except 5 per cent. basophils. The scalp lesions were typical sebaceous cysts.

DISCUSSION

Dr. Lieberthal at first thought the case was one of scleroderma, but after examining the section, he was willing to accept the diagnosis of granuloma annulare.

Dr. Stillians had thought of fibromas, but the clinical picture was not that of fibroma and on seeing the section he favored granuloma annulare, but was troubled by the pigmentation of the lesions.

Dr. Mitchell agreed with Dr. Stillians that the pigmentation was unusual. It was not the picture of granuloma annulare that he had studied histologically, but it fitted in with that described by Little as a keloid-like lesion.

Dr. Senear said he was unable to arrive at a diagnosis clinically but under the microscope he thought it was a case of granuloma annulare. He was not very familiar with this condition in the white race and not at all in the colored. Many disturbances took on increased pigmentation in the colored race, and this would not rule it out.

Dr. Ormsby agreed with Dr. Senear.

Dr. Eisenstaedt said the case would have to be considered one of granuloma annulare. The chief point was the absence of necrosis microscopically in any part of the lesion.

ALOPECIA. Presented by Dr. Senear.

Two Jewish brothers, aged 20 and 24 years, respectively, presented patches of baldness and stated that a brother and sister were similarly affected. The bald patches in the sister were first noticed at the age of 8, after which they were not so pronounced, but four years ago began to reappear. There was only one spot of baldness in each patient, and these were of recent origin. Before any local application was made they presented the usual appearance of alopecia areata, but one had been considerably changed by the application of Cutler's fluid. The bald spots had first been noticed a month before presentation, but the younger brother stated that a picture taken twelve years previously showed a bald patch.

DISCUSSION

Dr. Mitchell said that one or two hairs in the area on the right temple in one of the cases suggested the exclamation point, which was found in alopecia areata. The lesion in the other case might have been alopecia areata in the beginning, but it now appeared to be permanent alopecia. There was no evidence of scarring. He believed it was quite unusual to find so many members of the same family attacked with the same type of alopecia.

Dr. Quinn said that he had three cases in the same family, all in grown married sisters and brothers. In the youngest of the sisters the hair had all returned, while in an older sister the condition had gone on to total alopecia and a brother had lost about half of his hair. They lived in different parts of the city.

Dr. Senear stated that he first saw the case at the dispensary on Saturday, four days before presentation. At that time the young man stated that the patch had been present only three weeks and he painted the spot with Cutler's solution. He afterward brought his brother in and his scalp also showed the typical alopecia areata; Dr. Senear was then told of the sisters being similarly affected. He thought they were both cases of alopecia areata and presented the patients because of the occurrence of so many cases in one family.

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

A colored man, aged 32, presented multiple tumors which were slightly painful. About six years ago the patient had a generalized itching which responded promptly to treatment. Seven months ago he noticed a few nodules on the arms and scrotum. Four months ago two injections of arsphenamin were given, after which nodules became more pronounced and increased in number. The Wassermann reaction was negative.

The lesions consisted of multiple circumscribed nodules and plaques on the face, arms and hands, with smaller lesions at the nasolabial folds, angles of the mouth and on the chin. In addition to these, there were deeper hard nodules which were especially noticeable in the masseter muscles and around the wrists.

DISCUSSION

Dr. Lieberthal suggested a diagnosis of lichen planus hypertrophicus.

Dr. Ormsby thought the lesions looked more like tumor formation than lichen planus. The section under the microscope showed a well-defined new growth.

Dr. Senear said that the lesions on the arms in combination with the microscopic picture were more nearly subcutaneous sarcoid. There were giant cells in the section.

REPORT ON MISCELLANEOUS CASES.

Dr. Stillians reported on the case of recurrent psoriasis shown at the March meeting. He had put the patient on Fowler's solution and he had improved. He thought perhaps the fact that the lesions were not irritated by the chrysarobin would indicate that it was not such an acute eruption as was suspected, and that it would not be injured by the arsenic.

Dr. Senear said the baby with psoriasis showed marked improvement. The picture offered nothing new in the way of diagnosis and he still felt that it was psoriasis.

The young woman shown by Dr. Stokes at the January meeting with the numerous keloids had been kept under observation. An old record of her had been found in the office; she had been seen eleven years ago when a diagnosis of questionable pemphigus was made. A month ago she had a typical dermatitis herpetiformis, with bullous and papular lesions. When she was seen eleven years ago there was only one keloid present, in the scapular region.

Dr. Eisenstaedt asked whether the cases of eczema seen since prohibition went into effect were more frequent among men than before. One of his patients, who was accustomed to having several highballs a day, was eating huge quantities of sugar in candy, one-half to one pound a day, and presented himself with a pronounced eczema and much sugar in the urine. After prohibiting the candy the eczema cleared up.

Dr. Foerster thought there has been an increase in the cases of furunculosis. These patients had been taking larger quantities of sugar than usual, which was of interest in connection with Dr. Schwartz' recent work.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, March 23, 1920

George M. MacKee, M.D., *President*

POWDER STAINS TREATED BY CURETTING. Presented by Dr. Howard Fox.

E. P., a business man, aged 41, on Armistice Day (fourteen months ago) accidentally had a toy cannon discharged within 3 feet of his face. When first seen (two weeks later by Dr. Nilson) the right side of his face showed the presence of a large number of powder grains embedded in the skin of the cheek, nose, forehead, eyelids and ear. Some powder grains had previously been removed from the eye. During the past year about 190 individual powder grains had been removed by curetting under local anesthesia. About six grains from different parts of the face were removed at each sitting at intervals of a week or two. The skin was broken by a small eye curet, the powder grains picked up with a fine pair of forceps and snipped off with fine scissors. In contrast to the apparent damage done by each curettage, the resulting scars presented an unusually good cosmetic result.

DISCUSSION

Dr. Fordyce said that the method seemed to be good and the result was excellent.

Dr. MacKee inquired in regard to the kind of curet employed. It was difficult to curet normal skin unless the instrument was exceedingly sharp.

Dr. Howard Fox asked whether any of the members had had any experience in removing powder stains by any other method of treatment, such as injecting papoid, etc.

Dr. Winfield said that he had had a case many years ago and had tried various methods, but had not tried papoid. He finally employed a small curet, such as is used by the oculist, a small spoon-shaped curet, but he had to keep it very sharp. The result was satisfactory, but not as good as in this case.

Dr. Kingsbury said that the only satisfactory method was the mechanical method, and the result depends on the stage in which the condition is treated. As for papoid, it was worthless. He had had some experience with it years ago, but found it absolutely worthless.

Dr. Trimble congratulated Dr. Fox on the good result obtained, and said that he had also used a similar method for a number of years to remove lesions of this kind. He used a small curet, probably the same kind as that spoken of by Dr. Winfield. He desired to recall an interesting history of a patient now under his care who was suffering from a melanoma near the inner canthus of the eye. This patient had stated that sixteen years ago, due to the explosion of a firecracker, he had several small powder stains deeply embedded in the location mentioned. They were allowed to remain and about three months ago he noticed that they were getting larger and taking on a slightly verrucous appearance. He now has what seems to be a melanoma the size of a silver dollar on his temple directly over the powder stains.

LICHEN PLANUS SCLEROSUS ATROPHICUS (HALLOPEAU). LICHEN PLANUS MORPHOEICUS (CROCKER). Presented by Dr. Potter.

A woman, aged 50, apparently in good physical condition, had suffered from the condition presented for two months. There were typical lichen sclerosus lesions, located principally on the neck and shoulders. There was little itching associated with the lesions. An interesting point in connection with the case was that the woman was of a worrisome disposition.

DISCUSSION

Dr. Highman said he was much interested in seeing the violaceous rings which reminded one of the relationship with primary atrophy. It was an unquestionable case of the disease.

Dr. Wise agreed with the diagnosis, and thought it was a pretty example of the disease. It was almost the same as that published in his pioneer work by Ormsby, who also used the name of lichen morphoeicus. If in this case one could demonstrate a single lichen planus lesion, it would strengthen the diagnosis of lichen atrophicus. Without that the diagnosis was not easily made except by microscopic examination. If it were lichen atrophicus, the section would show an infiltration deep in the corium with a broad intervening band of connective tissue; whereas, if it were white spot disease, it would show no deep infiltration, only a condensation of the collagen, as in scleroderma.

Dr. MacKee said it was interesting to see the lesions in the various stages of evolution as well as of involution. There were flat, angular papules, violaceous in color, similar to those of lichen planus. It was the larger lesions that showed the sclerosis. Histologically they were not always distinguishable from scleroderma, for if one saw a papule in a late stage, the infiltration had disappeared and there was simply a sclerosed derma. Unless one obtained a history or a slide of an earlier lesion, it was sometimes difficult to make a differentiation histologically.

Dr. Potter said he had nothing to add to the discussion. He had not considered anything else but lichen sclerosis when he saw the patient. He thought the lesions showed, as had been stated by Dr. MacKee, all the stages of the condition, showing violaceous spots, hypertrophic areas and a few atrophic areas. He would endeavor to obtain a biopsy and report it at the next meeting.

DARIER-ROUSSY SARCOID. Presented by Dr. Williams.

A married Italian woman, 34 years of age, whose general health had been good, had lost 15 or 20 pounds in weight recently. The disease began on the left forearm two and a half years ago as firm subcutaneous nodules, the skin over which later became discolored as if from subcutaneous hemorrhage. There was little change until about five months ago, when fresh lesions appeared on the left arm and both legs. Subjective symptoms were confined to slight pruritus and slight tenderness on pressure. The patient presented lesions in various stages, from firm irregular subcutaneous nodules about an inch in diameter covered with skin showing only a trace of discoloration to dark blue-black, irregularly circular masses of about the same size, located apparently in the skin itself, with firm elevated borders and a center which was depressed and presented little resistance to the palpating finger. There had been no ulceration, but one lesion on the left leg was covered with a dry crust. Histologic examination confirmed the diagnosis.

DISCUSSION

Dr. Fordyce agreed with the diagnosis. He referred to the not infrequent association of papulonecrotic tuberculid with Bazin's disease, and spoke of a patient he had seen six years previously who then presented typical papulonecrotic tuberculid lesions of the lower extremities. She had recently consulted him again with deep tuberculous ulcers of the leg, together with more superficial lesions which clinically resembled sarcoid.

Dr. Highman declared that it was a remarkable and classic type of the disease. The involuting lesions on the left forearm nicely illustrated the peculiar chocolate brown color described by the discoverer of the disease. The histologic examination was characteristic, and there was no doubt about the diagnosis. Shortly before Boeck's death he published an article on his own type of sarcoid, in which he emphasized the name miliary lupoid as the better term, for he found tubercle bacilli in the lesions, so that if there was any similarity between the Boeck type and the Darier-Roussy type, it was easy to assume the relationship which Dr. Fordyce had brought out.

Dr. MacKee told of two interesting cases seen recently; both had multiple subcutaneous nodules all over the trunk; the underlying skin being adherent but not visually involved; both were diagnosed clinically as sarcoma, but histologically one proved to be sarcoma and the other a Darier-Roussy sarcoid or nodular tuberculosis of the hypoderm, as described by Wende. Clinically, however, the two could not be differentiated. Another patient had in addition to the sarcoid a lupus erythematosus of the face. He had treated a number of patients with Darier-Roussy sarcoid and also with the Boeck type of sarcoid; all had responded to the roentgen-ray treatment; all had required large doses—suberythema doses—and at times one treatment sufficed.

Dr. Highman remarked that the majority of these cases involuted spontaneously, but required some time to do so.

METASTASIS FROM EPITHELIOMA OF TRACHEA. Presented by Dr. Wise.

The trouble of Stephen McM., a man from Dr. Fordyce's clinic, aged 72, first began in the trachea five months previously, and at Bellevue Hospital a diagnosis of epithelioma of the trachea was made. He was there for three weeks, but received no specific treatment. As presented, he exhibited a large fleshy growth, the size of a fist, on the left side of the neck, which was probably a metastasis from a squamous-celled epithelioma of the trachea.

PARAFFINOMA. Presented by Dr. Kingsbury.

The history of this patient was not clear. The patient stated that ten years ago in St. Louis she had some treatment for lines in the face. It was evidently a case of paraffinoma. The case had already been presented at another meeting.

DISCUSSION

Dr. MacKee said that it was his impression that the paraffin was never absorbed, but that it stimulated connective tissue growth. The connective tissue grew all through the mass, separating the paraffin into small foci. This connective tissue stroma made it difficult to remove the paraffin.

Dr. Howard Fox said that this case reminded him of one he had shown a few years ago in which paraffin was injected by a quack to relieve a slight sinking of the cheek. All went well for some months until the patient tried applications of heat which caused the paraffin to melt and wander about the face with the production of a horrible result, similar to that seen in this patient.

Dr. Highman said the case reminded him of a similar one seen years ago in Paris in which leukemia had been strongly suggested by the purplish lesions.

GUMMA RESEMBLING EPITHELIOMA. Presented by Dr. Wise for Dr. Fordyce.

Delia R., 54 years old, born in Ireland, who had been in this country thirty-five years, a widow, showed a characteristic picture of an early tabes. The lesion below the left nostril had been present two months. It was circular, about the size of a dime, raised and infiltrated with ulcerated and rolled edges. There was no adjacent glandular enlargement. The complement fixation test for syphilis was + + + +.

The lesions had almost disappeared after two injections of arsphenamin and mercury salicylate.

DISCUSSION

Dr. Williams thought it was an epithelioma.

LESIONS ON THE TONGUE. Presented by Dr. Wise for Dr. Fordyce.

Anna B., a girl 10½ years old, for five years had had a lesion or lesions on the tongue, which never disappeared entirely, according to the mother. When the patient first came under observation the lesion was much more marked than as presented; it was then ulcerated and resembled more a leukoplakia or geographical tongue. The mother said the child suffered no pain, but on questioning the child her statements did not quite coincide with that idea.

DISCUSSION

Dr. Highman said that the obvious thing was first to rule out tuberculosis and syphilis. The condition could only be determined by a laboratory study, but it seemed to be traumatic.

Dr. Trimble agreed with Dr. Highman that tuberculosis and syphilis should first be ruled out, and that the condition could only be decided by a laboratory study.

Dr. Williams said that the tongue was too large for the size of the jaw, and in his opinion the lesion was caused by the pressure of the long tongue against the teeth. It was purely a chronic traumatism.

Dr. Wise agreed with Dr. Williams that the condition was probably caused by the pressure of the tongue against the teeth, and said that he would send the child to the dentist to learn what could be done for her.

EPITHELIOMA FOLLOWING ARSENICAL KERATOSIS. Presented by Dr. Wise.

A man, aged 42, from Dr. Fordyce's service at the Vanderbilt Clinic, had previously been presented. He had had pemphigus twenty years ago, and had then had his photograph taken by Dr. G. H. Fox at the Skin and Cancer Hospital. The assumption was that he had an arsenical keratosis at the sacrum, and it broke down into a squamous celled epithelioma.

DISCUSSION

Dr. MacKee said that as the patient had taken arsenic and presented arsenical keratosis of the palms it was presumed that the epithelioma had evolved from an arsenical keratosis.

Dr. Fordyce said in his opinion Dr. MacKee's conception of the case was correct. He had seen several cases of rather disseminated keratotic lesions in patients who had taken arsenic years previously. In one of these cases multiple epithelioma had developed at the sites of the keratosis. The statement of Hutchinson, that arsenic can cause keratoses which undergo malignant change has been repeatedly confirmed by subsequent observation.

Dr. Trimble said he agreed with everything said about the case except the assumption. It seemed hardly possible that a keratosis of the extent exhibited on this patient could arise from only six weeks of arsenical treatment. Perhaps the man's history was not absolutely accurate; he may have had some prescription containing arsenic without knowing its contents.

Dr. Wise said he should have demonstrated the keratosis on the soles and palms, where they were clearly of arsenical character. The diagnosis of arsenical keratosis of the palms had been made before the patient told them about the sacral lesion. Furthermore, there were two or three keratotic lesions in the lumbar region; in addition, he gave a history of arsenical keratosis preceding this, though he did not know it was a keratosis. The history of the short administration of the arsenic was remarkable, but the patient was an intelligent man and said he took Fowler's solution for his pemphigus. Another remarkable thing was that a man who had pemphigus twenty years ago should still be alive and well.

SYMMETRICAL PIGMENTED NEVUS OF THE AXILLAE. Presented by Dr. Fox.

L. G., a woman, aged 36, married, born in Russia, had come to the clinic for relief from a pityriasis rosea. On the middle of the extensor aspect of the right arm was a dark brownish, thickened, pigmented and hairy mole, about 4½ inches in length. In both axillae were symmetrical, almost perfectly circular, sharply bordered, brownish, pigmented, smooth lesions. The axillary hair was sparse. The nevi in the axillae were less elevated and thickened, and not as dark in color as the nevus on the arm. The patient thought the lesions in the axillae became lighter in summer, but said they never disappeared, and had been present since birth. The axillary lesions suggested at first glance an acanthosis nigricans. As the lesions were sharply confined to the axillae and had been present unchanged since birth, as there were no lesions of the mucous membranes or evidences of internal malignancy, the possibility of an acanthosis nigricans could not be properly entertained.

DISCUSSION

Dr. Williams said that it was an interesting case, showing another freak in nevi, but after having seen a few thousand men in the army go through the bathroom he had reached the conclusion that there was no limit to the manifestations of nevus. He had not before had any conception that they could be so various.

MINNESOTA DERMATOLOGICAL SOCIETY

Regular Meeting, May 5, 1920

S. E. Sweitzer, M.D., *President*

PITYRIASIS LICHENOIDES CHRONICA. Presented by Dr. Freeman.

A woman, aged 28, married, the mother of two healthy children, had had a generalized eruption for twenty-one years. Practically the entire body, except the face and hands, was involved. The eruption was brownish red in color. There were many pityriasis rosea-like patches and lichenoid papules. Itching and other subjective symptoms were entirely absent.

PITYRIASIS ROSEA RESEMBLING SYPHILIS. Presented by Dr. Sweitzer.

A young man presented a macular eruption over the body that in color bore a striking resemblance to the early eruption of syphilis.

DISCUSSION

Dr. Wright called attention to the presence of the eruption on the neck. He stated that the early, ungrouped syphilitic eruption is practically never seen on the neck. He had seen only one patient with the syphilitic roseola on the neck.

Dr. Butler stated that it is impossible to scrape off the scale in pityriasis rosea. Papular syphilids show a definite infiltration.

GRANULOMA PYOGENICUM. Presented by Dr. Armstrong.

A man, aged 26, about six months ago showed a typical granuloma pyogenicum on the pubes. At that time it was cut off and the base cauterized, but recurred and at the time of presentation was nearly an inch in length, resembling a cutaneous horn.

DERMATITIS EXFOLIATIVA. Presented by Dr. Michelson.

A man, aged 64, noticed last fall a red spot on his scalp. Scaling and itching were rather pronounced. The lesions did not become moist. In February the disease extended widely, involving the hands and genitocrural region. At the time of presentation the patient showed a generalized scaling eruption on the scalp, body and limbs. He complained of itching and burning. The general health was excellent. Urine examination was negative. Leukocyte count was 9,600 with 79 per cent. polymorphonuclears, 15 per cent. lymphocytes, 3 per cent. large mononuclears, 1 per cent. transitionals and 2 per cent. basophils. Hemoglobin was 94 per cent. The basal metabolism was normal. Blood chemistry showed blood sugar 0.115 per cent., creatin 2.51 mg., urea nitrogen 15.4, uric acid 7.1, and alkali reserve 6.5.

The microscopic section showed little change that was indicative. There was some hyalinization of the papillae and no lymphocytic infiltration.

DISCUSSION

Dr. Freeman thought the case was one of pityriasis rubra pilaris (Devergie).

Dr. Irvine called attention to the absence of branny desquamation and follicular involvement as seen in Devergie's disease.

Dr. Wright disagreed with the diagnosis of pityriasis rubra pilaris. The follicular lesions in pityriasis rubra pilaris are dirty yellow or grayish in color and not red.

Dr. Butler stated that this was a typical example of pityriasis rubra pilaris, and called attention to the follicular involvement on the hands and body.

Dr. Olson stated that he failed to see any follicular involvement on the hands, and thought the apparent follicular involvement on the body was cutis anserina, due to the fact that the patient felt cold.

HYDROA VACCINIFORME. Presented by Dr. Michelson.

A boy, aged 12, showed a disorder of eight years' duration, limited to the face and hands. No other member of his family had similar lesions. At the time of presentation there were numerous white scars on the face and hands. There were vesicles on the backs of the hands and on the ears. The backs of the hands showed extensive atrophy resembling senile atrophy. Freckles were present but no verrucous lesions or telangiectases. Blood examination showed a slight leukocytosis. The Wassermann reaction was negative.

The question of xeroderma pigmentosum was brought up, but the consensus of opinion was that this disease was ruled out by the absence of telangiectases, keratoses and photophobia.

SYPHILIS RESEMBLING SYCOSIS. Presented by Dr. Sweitzer.

The eruption in this patient, a man, aged 32, was papulopustular in character and limited to the beard. He had been treated for three years for sycosis by a number of doctors.

Book Review

THE TREATMENT OF SYPHILIS. H. SHERIDAN BAKETEL, A.M., M.D., New York, The Macmillan Company, 1920.

Baketel has compiled a volume for physicians who have not heretofore employed the intravenous method of injection in syphilis or those whose acquaintance therewith is limited. He uses extracts and abstracts of many excellent articles presented during the last decade, some chapters of the book being almost entirely so constituted. The chapters on the history and chemistry of arsphenamin comprise about fifteen pages and are rather technical. The charts are similar to, if not the same, as those used in advertising one brand of arsphenamin. Incidentally, one looks in vain under the heading of authorities quoted for Schamberg and his co-workers at the Dermatological Research Laboratories, whose contributions to American chemotherapy of arsphenamin could certainly not have been forgotten.

The use of various forms and preparations of mercury and iodids is mentioned, and there is a brief consideration of the pros and cons of intraspinal therapy as advanced by the leaders in this special field. Short chapters on the cure of syphilis, syphilitic reinfection and when a syphilitic may marry, close this volume.

The book has a distinct commercial flavor; it gives an incomplete presentation of the subject it purports to consider, and is not to be recommended. It is the sort of book on which one looks for a manufacturer's imprint.

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Wassermann Reaction and Miscarriages. H. Goodman, Surg., Gynec. & Obstet. **30:**368 (April) 1920.

Wassermann Reaction as Therapeutic Index for Syphilis. B. Oettinger, Am. J. Syphilis **4:**297 (April) 1920.

Wassermann Reaction, Standardization of. Comparative Study of Complement Fixation in Syphilis with Antihuman, Antichicken and Antisheep Hemolytic Systems. J. A. Kolmer, T. Matsunami and A. Rule, Am. J. Syphilis **4:**278 (April) 1920.

Wassermann Test. II. Significance and Value of Positive Wassermann Reaction in Leprosy. K. R. K. Iyengar, Indian J. M. Res. **7:**407 (Oct.) 1919.

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NOCARDIOSIS CUTIS RESEMBLING SPOROTRICHOSIS

REPORT OF A CASE

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Since 1898, when Schenk[1] reported his studies on refractory subcutaneous abscesses caused by a fungus possibly related to the sporotricha, over 200 proved cases and innumerable probable cases of sporotrichosis have been reported. Beurman and his associates made the bulk of these observations and while the clinical picture was different from that described by American authors and certain differences from the original fungus were noted, it is considered that these observations serve only to establish the identity of several subtypes of the same infection. Cases of sporotrichosis have been reported in this country by Hektoen and Perkins,[2] Hyde and Davis,[3] Hamburger,[4] Sutton,[5] Lewis,[6] Pusey,[7] Stelwagon,[8] Olson,[9] Blaisdell,[10]

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[1] Schenk, B. R.: On Refractory Subcutaneous Abscesses Caused by a Fungus Possibly Related to the Sporotricha Bull. Johns Hopkins Hosp., December, 1898, p. 286.

[2] Hektoen, L., and Perkins, C. F.: Refractory Subcutaneous Abscesses Caused by Sporothrix Schenckii, a New Pathogenic Fungus, J. Exper. Med. **5**:77 1900.

[3] Hyde, J. N., and Davis, D. J.: Sporotrichosis in man, with Incidental Consideration of Its Relation to Mycotic Lymphangitis in Horses, J. Cutan. Dis. **28**:32 (July) 1910.

[4] Hamburger, Walter W.: Sporotrichosis in Man, J. A. M. A. **59**:1590 (Nov. 2) 1912.

[5] Sutton, Richard L.: Sporotrichosis in America, J. A. M. A. **55**:2213 (Dec. 24) 1910.

[6] Lewis, Dean: Blastomycosis and Sporotrichosis, Surg. Clin. Chicago **1**:1125 (Dec.) 1917.

[7] Pusey, W. A.: The Therapeutic Use of Refrigeration, Particularly with Solid Carbon Dioxid, J. Cutan. Dis. **28**:352, 1910.

[8] Stelwagon, H. W.: Short discussion of the Hyde and Davis Paper, J. Cutan Dis. **28**:144, 1910.

[9] Olson, G. M.: A Case of Sporotrichosis in North Dakota. Probable Infection from Gophers, J. A. M. A. **59**:941 (Sept. 21) 1912.

[10] Blaisdell, J. H.: A Clinical and Histopathological Report of the First Case to Be Published in New England, J. Cutan. Dis. **35**:452 (Aug.) 1917.

Moore,[11] Laine[12] and others and the clinical picture in practically every instance has been that of the sporotrichotic chancre with an ascending lymphangitis. In most of these cases, the sporotrichium of Schenck was demonstrated. Therefore, a case that agrees with the description of sporotrichosis clinically, but found to be caused by an organism other than the sporotrichium of Schenck, is considered worthy of a special report.

REPORT OF CASE

History.—In July, 1919, C. L., a man, single, aged about 50 years, a coal miner, was referred for diagnosis and treatment. He was suffering from a number of inflammatory lesions extending in linear fashion from the base of the left thumb to a point slightly above the bend of the elbow.

The following rather incomplete history was obtained. About six months before presenting himself, there appeared at the base of the left thumb "a small pimple" to which no attention was paid. In about two weeks the lesion developed to about the size of a pea and a drop of pus formed in it. This was pricked with a pin and various home remedies applied without materially affecting the lesion, which developed into an indolent ulceration one-half inch in diameter. About this time a second "pimple" appeared close to the proximal side of the first one. This lesion was treated in the same manner as the original focus with the same result. In about a month a third lesion appeared close to the second. This one developed into a larger lesion than either of the two earlier ones, and finally discharged a considerable amount of thick pus. Others appeared at intervals until a complete chain of lesions in various stages of development extended from the site of the chancre to the latest lesion which had appeared as a "little pimple or lump" within the preceding seven days. At no time had the patient's general health been affected, and the lesions themselves gave little discomfort.

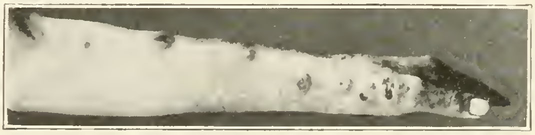

Fig. 1.—Nocardiosis of the hand and arm of author's patient.

Appearance of the Condition When First Seen.—The site of the early lesions was occupied by a superficial indurated ulceration, irregular in outline, evidently formed by confluence of two or more smaller ulcers. The edges were ragged and the base was covered with an indolent appearing granulating tissue. Extending from this point to just above the bend of the elbow was a chain of hazelnut sized inflammatory nodules with soft centers, the two nearest the ulcer being of a doughy consistence. Those nearest the bend of the elbow were firm and were graded in size from the largest of the lesions

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[11] Moore: Reporting a Case at the Meeting of the Chicago Dermatological Society, J. Cutan. Dis. **35**:609, 1917.

[12] Lain, E. S.: Sporotrichosis, State M. J. Oklahoma M. A. **13**:41 (Feb.) 1920.

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to the week-old lesion, which was about the size of a split pea, firm to the touch, moderately inflammatory and firmly fixed in the skin. None of the lesions were as tender as they appeared to be.

Bacteriology.—Under aseptic precautions, one of the large soft unbroken lesions was opened and various culture mediums inoculated. After forty-eight hours, at room temperature, there appeared on agar several grayish white pinhead sized colonies, rather dense at the center, with a fine radiating fringe. This was found to be made up of a mass of tangled branching threads, bearing small granules. Older cultures showed the presence of these fine granules between the threads.

Histopathology.—The youngest lesion which, according to the patient, was about a week old, was removed and paraffin sections made at the W. H. Singer Memorial Laboratory under the supervision of Drs. S. R. Haythorn and G. R. Lacy, to whom I am also indebted for the original bacteriologic work. No changes of moment were noted in the epidermis. In the derma there was a more or less circumscribed infiltration rather thin superficially and becoming more dense at about the level of the coil glands. The tissues generally were intensely edematous and in places the collagenous tissues showed a tendency toward basic staining. The blood vessels were more or less dilated and in places surrounded by a moderate cellular infiltration. The focus of the infection was deep in the derma, in and about markedly dilated lymphatic spaces and vessels. The infiltration was largely lymphocytic or round cell in type, there being, however, a goodly number of epithelioid cells and a few polymorphonuclear leukocytes. One ill-formed giant cell was noted. By the Gram-

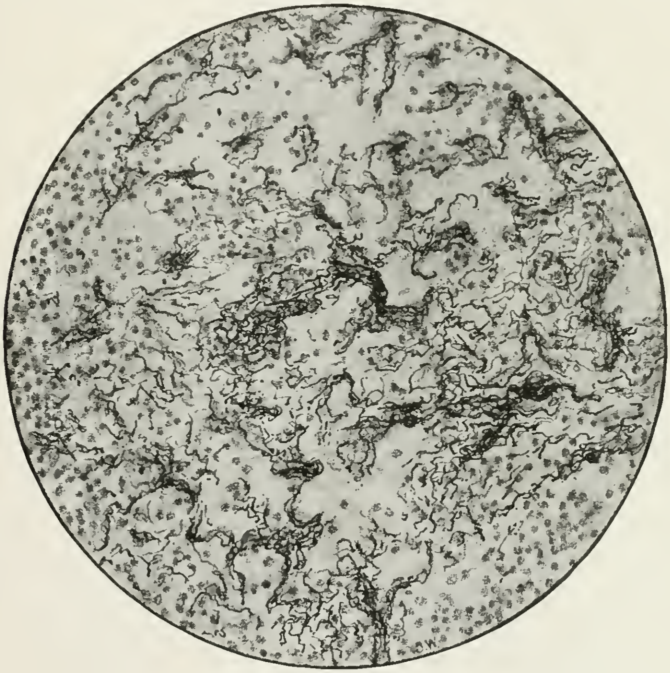

Fig. 2.—Arrangement of the threads and the infiltration.

Weigert method of staining, numbers of parallel and tangled threads were demonstrated in and about dilated lymphatic vessels and spaces at the focus of infection mentioned above.

Classification of the Organism.—Dr. W. L. Holman of the department of bacteriology at the University of Pittsburgh has supplied the following notes:

"The micro-organism grown from and seen in the tissues of this case should be classified under the Actinomycetaceae.[13] The Actinomycetaceae is divided into two species—Actinomyces, including the anaerobic species, and Nocardia, including the common saprophytic soil forms, as well as a number of pathogenic species.

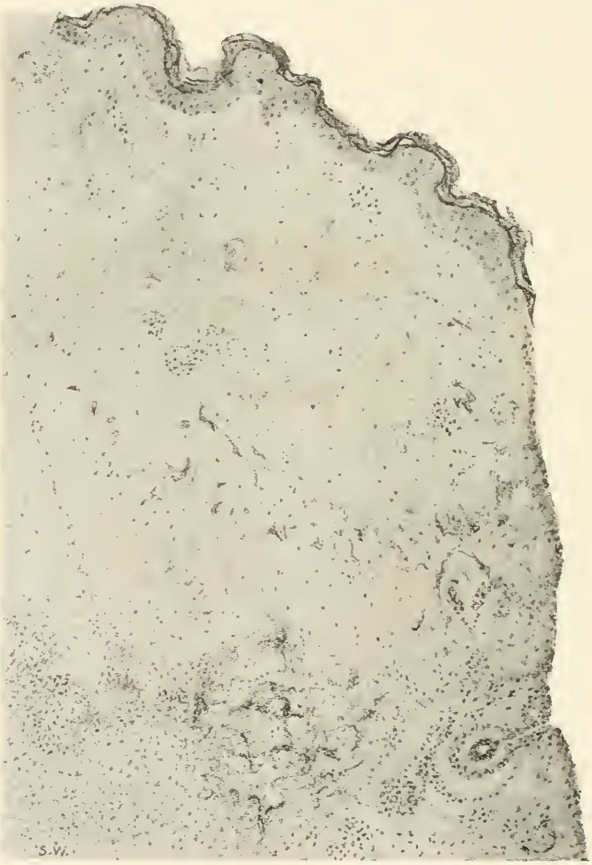

Fig. 3.—Low power drawing showing location of the focus.

"The further classification of the Nocardial strain here reported is practically impossible in the present state of our knowledge and the confusion of

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13. Breed and Conn: Nomenclature of the Actinomycetaceae, J. Bacteriol. **4**:585, 1919. Foulerton: Nature of Parasites of Leprosy and Tuberculosis (a Discussion of Streptothrix and Allied Forms), Brit. M. J. **2**:300, 1912.

nomenclature. The morphologic picture of tangled, branching threads, with granules or 'spores' in the threads or, in older cultures, free in the medium, the nodular appearance and the manner of growth on and in mediums, all indicated that it is closely allied to the air Nocardia. The presence of thread formation in the tissues, without spore forms, precludes it being grouped with the Sporothrix, Coccidioides or Blastomyces. Further, it differs radically from all of these in microscopic morphology from cultures and the type of colony developed on mediums.

"The Sporothrix is a closely allied but higher fungus with branching, septate mycelium which forms yeast-like 'spore' bodies, within and budding from the mycelium. In the tissues it shows, almost exclusively, these elongated yeast forms. The so-called spores of Nocardia resemble short rods or coccoid forms of the organism and are much smaller than the yeast-like 'spores' of Sporothrix. Streptothrix has been dropped from the nomenclature of these thread forms."

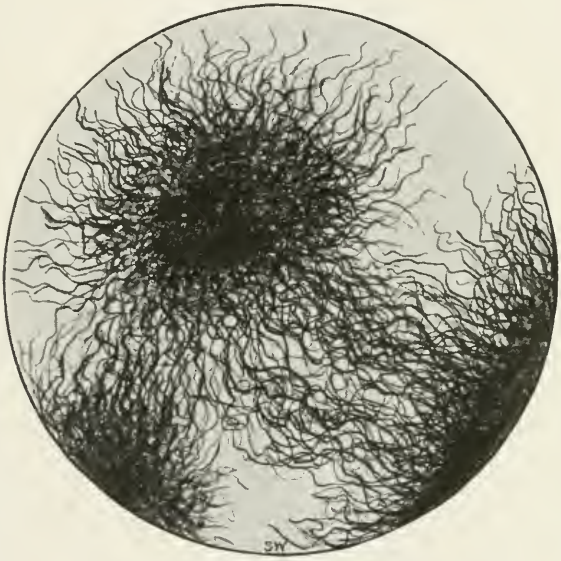

Fig. 4.—A four day old hanging drop culture.

Further Notes on the Case.—When first seen, a clinical diagnosis of sporotrichosis was made, and the patient was supplied with a saturated solution of the iodid of potassium. He was instructed to take ten drops in water three times a day, increasing the dose one drop a day. Nothing else was done except to apply simple protective dressings, and the patient made an uninterrupted recovery.

HISTORICAL

Under the term nocardia is included a considerable number of more or less closely related organisms, the pathogenicity of which have been demonstrated in several different clinical conditions, although there are also many nonpathogenic members of the family. The name is applied to the group on grounds of priority because

Nocard first described such an organism, which he isolated from the superficial abscesses of cattle suffering from farcy.

For a concise summary of the subject of nocardiosis, the reader is referred to an article by J. H. Wright.[14] The process in most of the cases at that time had been in the lung or had originated there. Signs of empyema were present in two cases, in one of which there was an inflammatory fluctuating tumor on the external aspect of the chest wall. In two cases there were multiple metastatic abscesses in the subcutaneous tissues with symptoms of pyemia. In one of these, infection with the bacillus of glanders was suspected. In a few cases the process has been essentially of the character of a terminal infection. In three of the cases there was abscess formation in the brain. In the case of subacute peritonitis with gastrotomy, the prominent symptom was diarrhea.

In 1913, Potron and Thiry [15] reported a case of nocardiosis involving the skin of the neck with small vesicles from which pus escaped causing the formation of small yellowish crusts, giving the appearance of impetigo. In the center of the inflamed area was a hard tumor, pressure on which caused the escape of pus through a small fistula. A smaller growth was near it. The organism was grown on various mediums and was recovered from experimental lesions in animals. This patient recovered under the administration of potassium iodid. About the same time Steele and Lee [16] isolated a nocardia in the sputum of a patient with pneumonia and empyema. In 1914 Davis [17] reported another pulmonary case. In 1916 Macfie [18] discussed trichonocardiosis, a disease affecting the hair shafts of the axillae and groin. The organism described does not agree in detail with the one from my case, but evidently belongs to the same group. Pijper [19] recovered a nocardia from a case of bronchitis, and reported indifferent results from vaccines. In 1918, de Korte [20] reported a case involving the external ear with a dusky red, brawny swelling extending about 2 inches around the insertion of the ear. The patient ascribed the

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[14] Wright, J. H.: Nocardiosis, in Osler, Modern Medicine, 1907, p. 340.

[15] Potron, M., and Thiry, G.: Pyodermatomycose provoquee par un "Nocardia," Rev. méd. de l'Est **45**:159 and 198, 1913.

[16] Steele, A. E.: A Case of Infection with Nocardia, Boston M. & S. J. **169**:502 (Oct. 2) 1913.

[17] Davis, D. J.: An Acid-Fast Streptothrix (Nocardia), Chicago Path. Soc. Trans. **9**:177, 1914-1915.

[18] Macfie, J. S.: A Fourth Variety of Trichonocardiasis, Ann. Trop. M. & Parasitol. **10**:283, 1916.

[19] Pijper, A.: Nocardiosis, Med. J. S. Africa **12**:141, 1916-1917.

[20] De Korte, W. E.: Nocardia Cylindracea; a South African Otomycosis, Ann. Trop. Med. & Parasitol. **11**:265, 1917-1918.

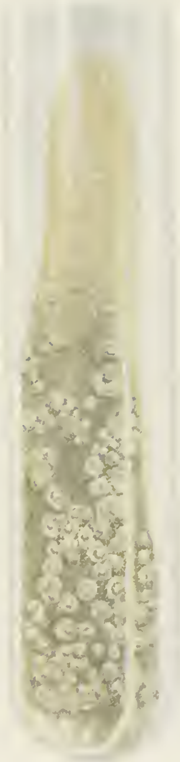

Fig. 5.—An old culture.

trouble to a prick on the ear with forage. Iodids caused improvement but did not cure, recourse being had to an autogenous vaccine.

Christopherson[21] reported a case of primary nocardiosis of the lacrimal gland. Other cases are reported in the literature, but the original articles are not available.

I am indebted to Dr. O. Klotz of the Department of Pathology, University of Pittsburgh, for the drawings.

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[21] Christopherson, J. B., and Archibald, R. G.: Primary Nocardiosis of the Lacrimal Gland, Lancet **2**:847, 1918.

THE HISTOGENESIS OF MOLLUSCUM CONTAGIOSUM *

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In a paper by Wile and Kingery, presented at the last annual meeting of the American Dermatological Society, were detailed a series of experiments directed toward a demonstration of the etiologic agent of molluscum contagiosum. As a result of their studies, these authors were able to show that the lesions of this disease can be produced experimentally from the sterile filtrate of molluscum lesions, thereby justifying their conclusion that molluscum contagiosum is caused by a filterable virus. The technic of these experiments, as carried out on themselves and their assistants, was comparatively simple. Molluscum lesions were removed by curettement, ground up in a mortar containing a small amount of sterile saline, and the resultant mash passed through the finest Berkefeld filter under negative pressure. The filtrate thus obtained, which produced no growth on all ordinary culture mediums, was injected intracutaneously into human subjects, at the points of predilection for the development of this disease. After an incubation period varying from twelve days to three weeks, definite papular lesions developed at the sites of the injections. These lesions rapidly took on the clinical characteristics of molluscum contagiosum. Those examined histologically, after a developmental period of eight weeks, presented the unmistakable picture of the disease, including the so-called "molluscum bodies." The subjects of these experiments were under daily observation and histologic study was undertaken at short intervals during the entire evolution of the lesions. In this way material was obtained including every developmental phase of the lesions, from the earliest pinpoint papule, up to the mature stage with its waxy appearance, the central umbilication, etc. The material thus studied offered an unusual opportunity for the investigation of lesions whose histogenesis has been a debated question since the time of Bateman's original description of the disease. It is on a critical examination of this material that the present study is based.

TWO THEORIES REGARDING ORIGIN OF MOLLUSCUM CONTAGIOSUM

The opposing views of many leading investigators, regarding the peculiar histologic picture presented by molluscum contagiosum, are

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

found recorded frequently in the literature on this disease. Out of these controversies two preeminent theories have been developed, which are today used in an attempt to explain the origin of these lesions.

Theory of Pilosebaceous Origin.—The first of these views to be advanced was to the effect that the lesions of this disease are related to the pilosebaceous apparatus. Engel[1] was among the foremost to take a definite stand on this interesting phase of the question. As the result of a series of observations, he stated his belief that the molluscum tumor was to be regarded as an enlarged sebaceous gland. This view was strengthened a few years later, when Virchow[2] published the results of his investigations of this disease. He interpreted the histologic picture as a lobulated glandular epithelioma, arising from the hair follicle. He further likened the molluscum bodies to fat-like

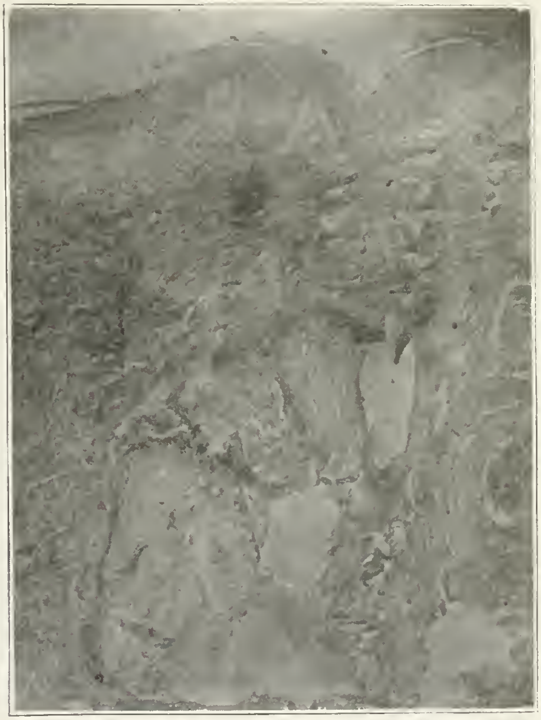

Fig. 1.—Early pinpoint size experimental lesion, showing beginning localized acanthosis and related gland structures.

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[1] Engel: Ztschr. d. k. k. Gesellschaft der Aerzte in Wien **2**:408, 1844; abst. White and Robey: Molluscum Contagiosum, J. Med. Research **7**:25, 1902.

[2] Virchow: Molluscum Contagiosum, Berl. med. Gesellschaft Sitzung, Dec., 1864; Berl. klin. Wchnschr. **2**:34, 1865.

globules surrounded by a double-contoured rim, which resisted the action of water and acids. A few years later Kaposi's[3] views were published. He was one of the first to agitate the contagiousness of the disease and at the same time he stated his firm belief in the follicular origin of the tumors. The following year Vidal[4] likewise expressed himself as believing the tumor to be of pilosebaceous origin, and added the suggestion of a colloid degeneration of the cells. The papers of Renaut,[5] Crocker,[6] Hebra,[7] and Benda[8] appeared shortly afterward, in which each, while placing different interpretations on the molluscum bodies, firmly stated his belief that these tumors arise always in connection with the pilosebaceous apparatus. Among the list of supporters of this view must also be included the names of Erasmus Wilson,[9]

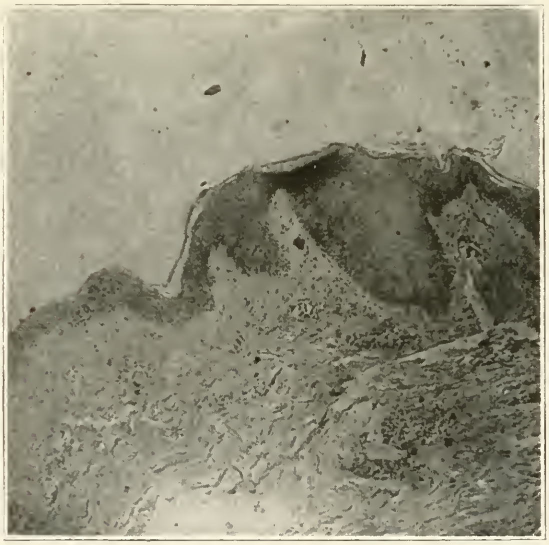

Fig. 2.—Experimental molluscum lesion, a few days later; acanthosis more marked.

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[3] Kaposi: Ueber das sogenannten Molluscum Contagiosum, Vierteljahresschrift f. Dermat. u. Syphilis **4**:333, 1877.

[4] Vidal: Soc. de Biol., Seance du 15 juin, 1878, Progres méd. **0**:478, 1878.

[5] Renaut: Anatomie pathologique de l'acne varioliforme, Ann. de dermat. et syph. **1**:397, 1880.

[6] Crocker: Diseases of the Skin, London, H. K. Lewis, 1893, p. 479.

[7] Hebra, F.: Diseases of the Skin, Including the Exanthemata **1**:131, trans. by H. Fagge, London.

[8] Benda: Untersuchung ueber die Elemente des Molluscum Contagiosum, Dermatol. Ztschr. **2**:195, 1895.

[9] Wilson, E.: Diseases of the Skin, London, 1842, p. 341; ibid.: Diseases of the Skin, Philadelphia, 1863, p. 653.

Rokitansky,[10] Tilbury Fox,[11] Hutchinson [12] and others. Minor differences of opinion are to be found in the publications of these investigators; yet, in the main, it is to them that we owe the belief, still shared by many authorities, that the lesions of this disease are always, in some way, related to the pilosebaceous apparatus of the skin.

Theory Regarding Origin of Molluscum Contagiosum in Rete Layer of Epidermis.—Coincident with the studies and investigations mentioned above, however, other and equally reputable investigators placed an entirely different interpretation on the microscopic picture of these tumors. For them the lesions were never related either to the follicles or the sebaceous glands, but were due to a pathology concerning only the rete layer of the epidermis. As early as 1848, only a few years after the article by Engel, von Barensprung [13] described the bodies making up these tumors as epidermal cells which had undergone a peculiar degeneration. He furthermore stated his belief in their nonfollicular origin. A few years later Retzius [14] concluded, after a series of observations, that the tumors were never related to the pilosebaceous apparatus, but owed their origin entirely to the epidermis. Shortly thereafter Boeck,[15] after a careful study, entirely denied the sebaceous origin of the lesions, because fat is never detected in the cells. This reasoning, however, is hardly more tenable than would be a similar objection to the origin and relation of a tumor of the pancreas because of the absence of pancreatin in the cells of such a new growth. The absence of fat might be more easily explained by the changes through which the cells must pass before molluscum bodies are obtained. The papers of Lukomsky [16] and O. Simon [17] then followed, and offered separately, as an explanation, an enormous proliferation of the rete cells, resulting in the peculiar tumor formation seen. A few years later the subject was carefully presented in a paper by Geber,[18] in which

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[10] Rokitansky: Pathologische Anatomie, Ed. 3, Vienna, Braumuller, **2**: 79, 1856.

[11] Fox, T.: Case Report, Clinical Society of London, April, 1872, Brit. M. J. **2**:538, 1872.

[12] Hutchinson, J.: Lectures on Clinical Surgery, London, J. and A. Churchill, 1878.

[13] Von Barensprung: Beitrage zur Anatomie und Pathologie der Haut, Leipzig, 1848, p. 43.

[14] Retzius: Ueber Molluscum Contagiosum, Deutsch. Klin. **23**:450, 1871.

[15] Boeck: Ueber Molluscum Contagiosum und die sogenannten "Molluscumkorper," Vierteljahresschrift f. Dermatol. u. Syphilis **2**:23, 1875.

[16] Lukomsky: Ueber Molluscum Contagiosum, Virchows Archiv. **65**:145, 1875.

[17] Simon, O.: Ueber Molluscum Contagiosum, Vierteljahresschrift f. Dermatol. u. Syphilis **3**:400, 1876.

[18] Geber Ein Fall von Epithelioma molluscum (Virchow) universal mit besonderer Rucksicht auf dos Wesen deiser Frankheit Pest, Med. chir. Presse, Budapest, 1882, pp. 685, 703.

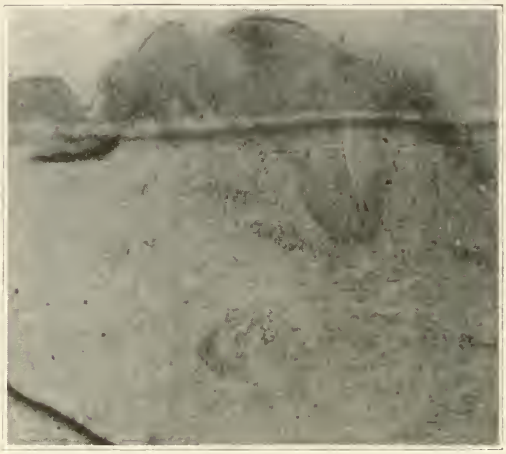

Fig. 3.—Early experimental molluscum lesion, showing involvement of follicle, hair remnants and related gland.

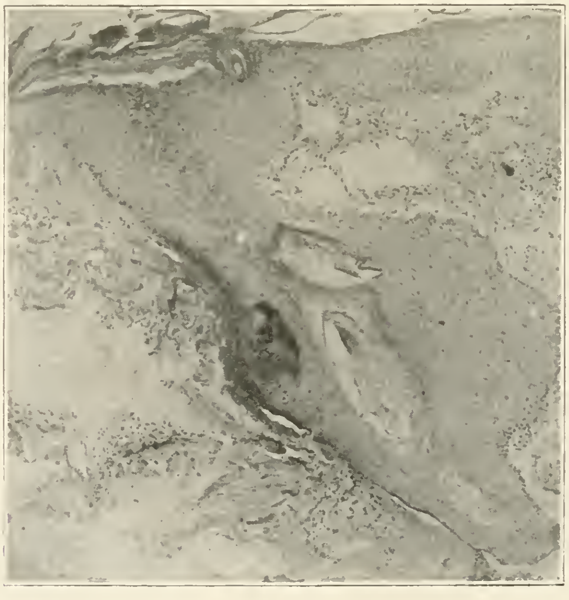

Fig. 4.—Continuation of follicular acanthosis and beginning cellular degeneration.

he attempts to trace the evolution of the rete cells into the molluscum bodies. Still later Neisser,[19] 1882, Stanziale,[20] 1890, and McCallum[21] in 1892, published papers, and among other observations stated their firm belief in the nonfollicular origin of the tumors. In 1896 Unna's[22] histopathology appeared with a most thorough elucidation of the subject. In this Unna suggested the term "epithelioma contagiosum," and stated that he did not believe the tumors to be of sebaceous origin because he had never seen any sebaceous material in the tumor tissue. This reason, however, seems to prove the point no more than that offered by Boeck and is, I believe, open to the same objections. Finally, a most scholarly review of the subject, presenting previous and contemporary opinions, has more recently been published by White and Robey.[23] Besides those mentioned above, the names of Campana,[24] Torok,[25] Klebs and Kromayer[26] must be added to those who believe in the nonfollicular origin of the lesions of the disease.

Such, then, have been the theories of the histogenesis of molluscum contagiosum up to the present time. Two explanations, one almost diametrically opposed to the other, yet each supported by more than one of the leading investigators of their time. Similarly, differences of opinion have arisen through attempts to explain the derivation and origin of the so-called "molluscum bodies." This, and other ques ions, have not been included in the present study, in which the subject of histogenesis only has received consideration. So far as the literature reveals, the opportunity for investigation of material similar to that of the present study has never presented itself in the past. This fact, it is believed, justifies a fairly detailed account of the changes as observed in the development of lesions experimentally produced.

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19. Neisser: Ueber das Epithelioma (sive Molluscum) contagiosum, Vierteljahresschrift f. Dermatol. u. Syphilis **15**:553, 1888.

20. Stanziale: Gior. Internazional de Sc. Med. n. s. 1890, n. s. **12**: 321, 1 pl. Contributo sperimentale anatomo-patologico e batteriologico all studio del mollusco contagioso di Bateman.

21. MacCallum: Histology of Molluscum Contagiosum, J. Cutan. & Gen.-Urin. Dis. **10**:93, 1892.

22. Unna: Histopathology, Diseases of the Skin, Walker's trans., Edinburgh, W. F. Clay, p. 793.

23. White and Robey: Molluscum Contagiosum, J. Med. Research **7**:255, 1902.

24. Campana: Sui globi del Mollusco contagioso, Gior. ital. d. mal. ven. **21**:37, 1886.

25. Torok and Tommasoli: Ueber das Wesen des Epithelioma Contagiosum, Monatsh. f. prakt. Dermat. **10**:149, 1890.

26. Klebs: Psorospermirn im Innern von thierschen Zellen, Virchows Arch. f. path Anat. **16**:188, 1859.

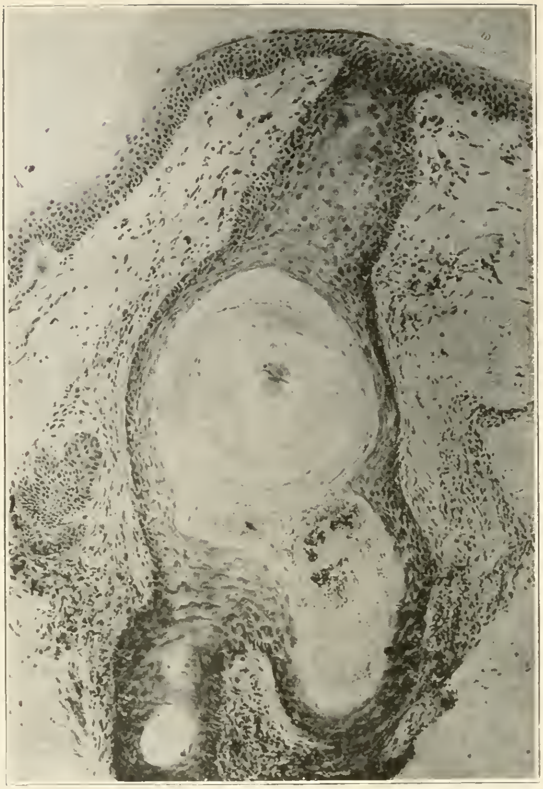
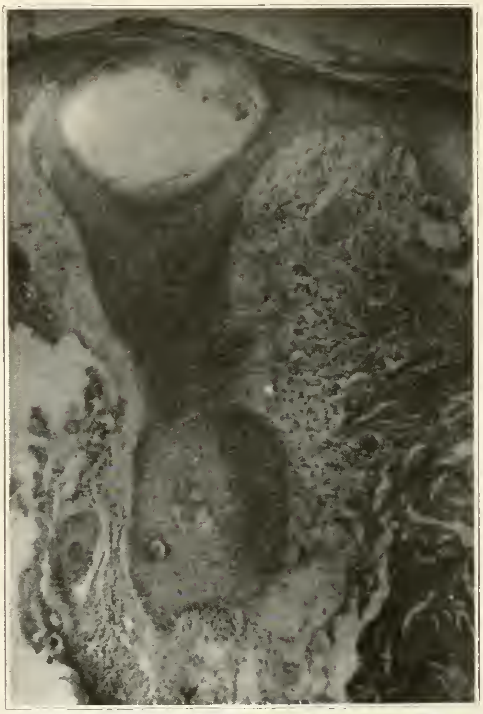


Fig. 5.—Experimental lesion few days older, showing early cavity formation and cellular changes.



STUDY OF MOLLUSCUM CONTAGIOSUM EXPERIMENTALLY PRODUCED

As stated before, the development of these lesions was under daily observation, so that clinical and histologic examinations were possible as frequently as developmental changes warranted. Approximately twelve days following the injection of the sterile filtrate, one of the patients developed small papular lesions, surrounded by a slightly erythematous zone. These rapidly took on characteristics, making a clinical diagnosis possible. One of several lesions excised at this time are shown in Figures 1 and 2. Apparently, the first change occurring is that of an extremely small, localized acanthosis, the process resulting in a downward bulging of the epithelium, the increase in thickness being due chiefly to malpighian changes. Apparently, this change continues for some time, the acanthosis becoming more marked, the rete pegs being gradually obliterated, and the process encroaching on the underlying cutis. A few days later, however, serial sections show a factor not present in Figures 1 and 2, i. e., that this acanthotic change involves the follicular wall, a fact evidenced by the hair sheath remnants present and the glandular structures deeper in the section (Fig. 3). Sections a

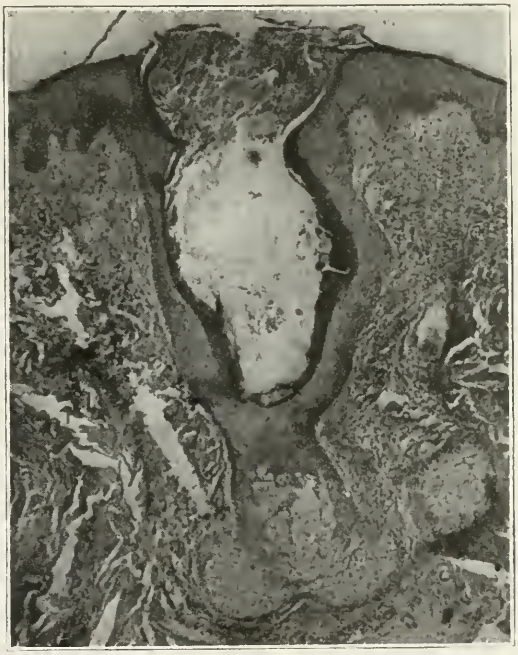


Fig. 7.—Experimental lesion showing early umbilication, epithelial pocket formation, cellular debris, and related glandular structures.

short time later show a still more extensive involvement of the follicular apparatus (Figs. 4 and 5). The experimental lesions developed fairly rapidly in certain instances, and by the twenty-first day, in one case, had assumed definite papular proportions, presented a waxy appearance, and in not a few a central umbilication was evident. Again serial sections were examined (Figs. 6, 7 and 8). In addition to the follicular acanthosis above described, a peculiar cellular degeneration had begun to appear in the central portion of the process. At first these changing cells stain not unlike those undergoing hyperkeratinization. Soon, however, these centrally located, deep-staining cells undergo further degeneration, and in the course of a few days the

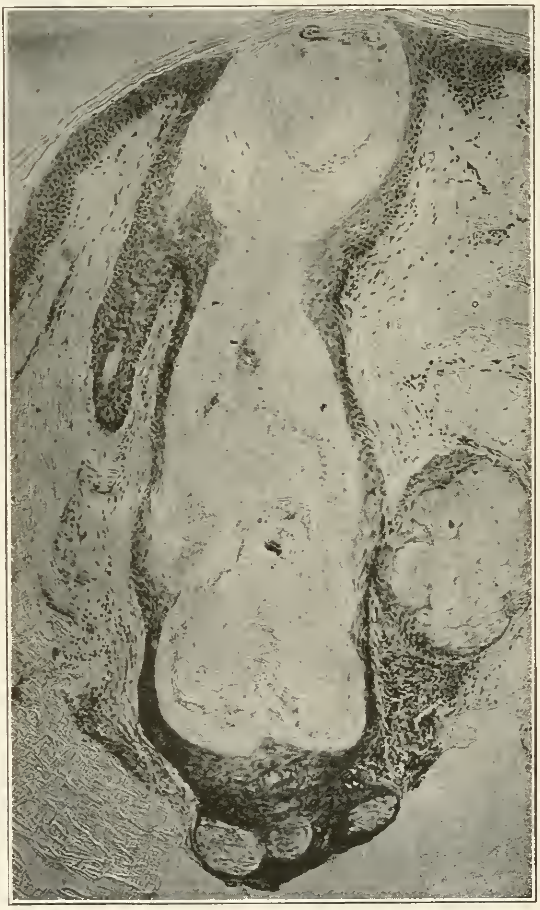


Fig. 8.—More extensive follicular involvement, marked epithelial pocket formation, etc. A lesion clinically typical of molluscum contagiosum.

process assumes the true outline of molluscum lesions (Figs. 9, 10, 11, 12 and 13). In section, the basal cell layer remains apparently unchanged and intact, and in addition there is epithelial pocket formation with a central cavity containing for the most part cellular debris. Apparently, the so-called molluscum bodies develop relatively late in the disease, as in none of the specimens examined up to this time were the bodies present, although the lesions were clinically typical of the disease. Objective change was gradual from this time on. The lesions slowly increased in size, and one after another, without exception, took on the peculiar waxy color, developed a central umbilication, and from time to time the patients complained of pruritis. It was also an interesting observation that new lesions began to appear outside the sites of injection, an occurrence suggestive of the contagiousness of the condition and its dissemination by the trauma incidental to scratching. The lesions at this time were in the sixth week of development, and as the picture had apparently changed so little, biopsies were suspended for a number of days. Approximately eight weeks following the beginning of the experiment, a few more clinically typical lesions developing at the sites of injection, were removed. Sections of these

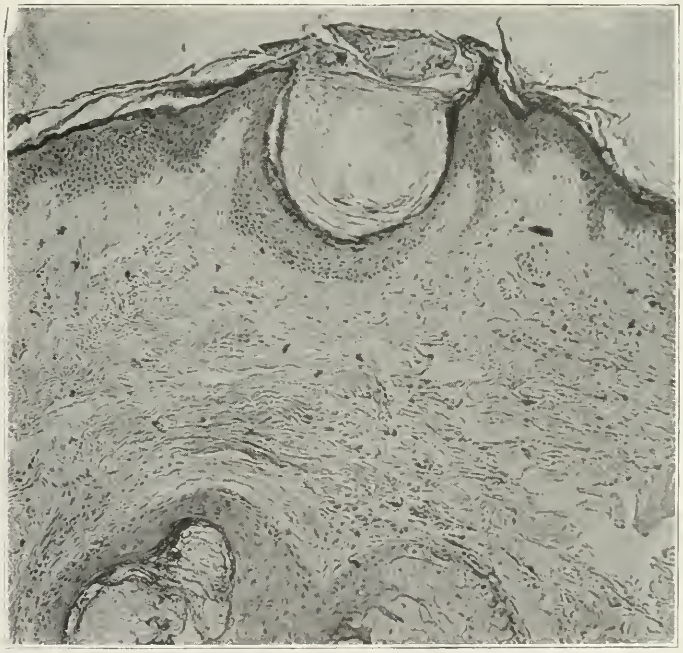


Fig. 9.—Somewhat later stage, well formed capsule, cellular degeneration, pilosebaceous structures.

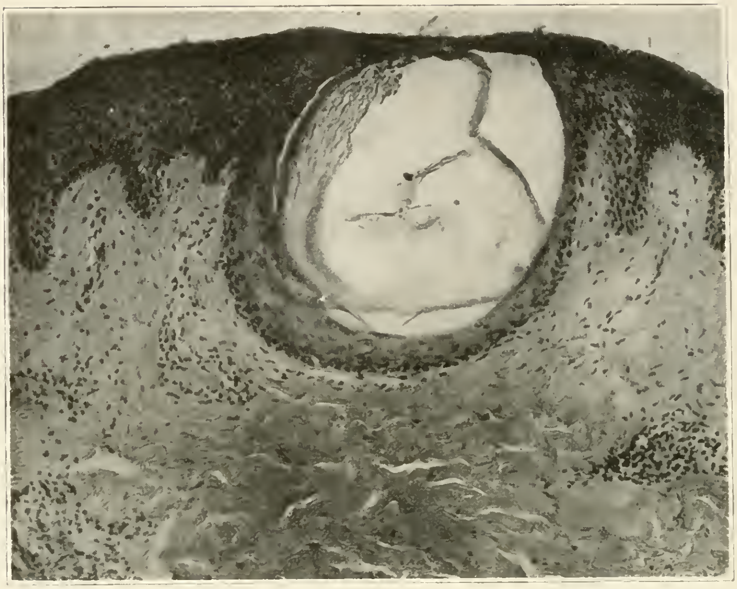


Fig. 10.—Slightly older lesion, showing gradual growth of epithelial pocket.

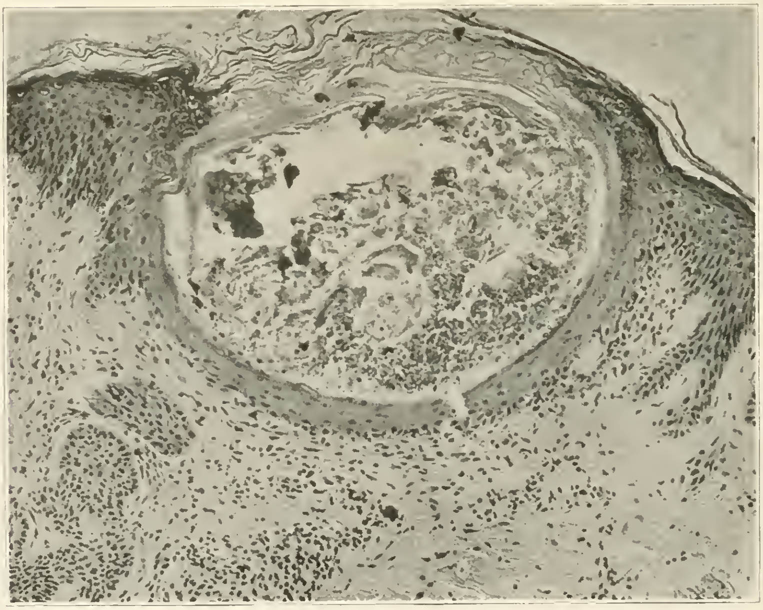


Fig. 11.—Well formed experimental lesion of molluscum contagiosum, typical except for absence of true molluscum bodies.

lesions are shown in Figures 14 and 15. A detailed description of these typical lesions is unnecessary. In Figure 14 the peculiar degeneration of this disease appears below the surface, being attached by an epithelial pedicle of unchanged cells. In the tumor itself, the basal cell layer is apparently little changed, the peculiar metamorphosis becoming more evident as the central portion is approached. The epithelial pedicle extending downward from the surface, in view of the relation shown in previous earlier sections is, I believe, the unaffected portion of the follicular wall, in tangential section. In Figure 15, a more central section, the process extends to the surface, umbilication is evident, and the adult stage is evidenced by the presence of the molluscum bodies.

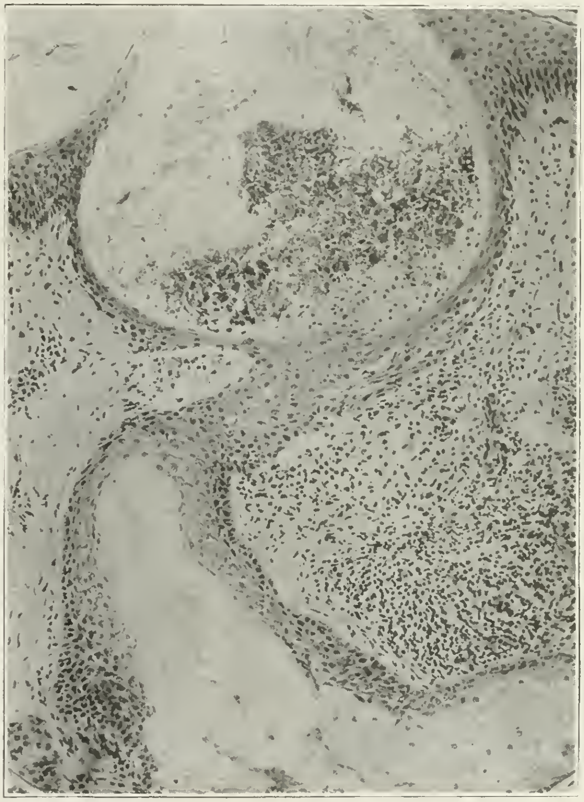


Fig. 12.—Experimental molluscum lesion, showing relation of pilosebaceous apparatus.

To review briefly, the observations recorded above are from lesions developing at the sites of injections of the sterile filtrate of the lesions of molluscum contagiosum. The described changes are as seen in the

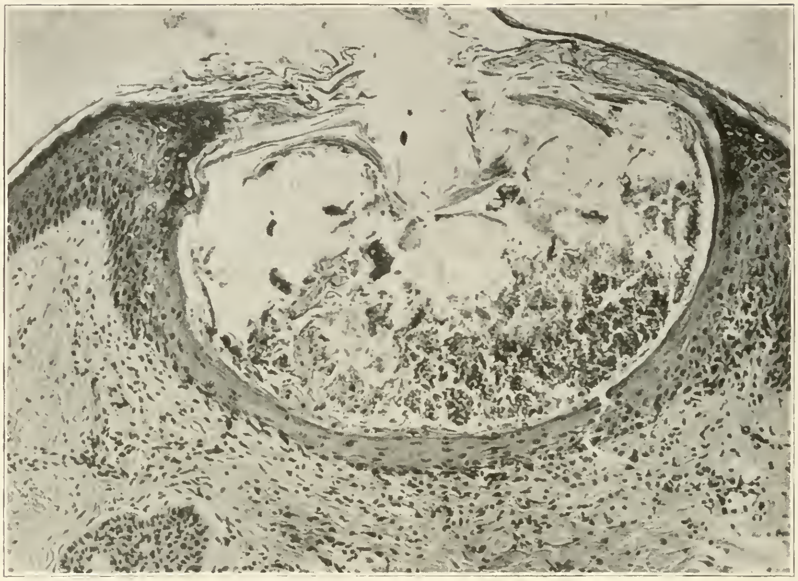


Fig. 13.—Experimental molluscum lesion, approximately six weeks old, the typical picture, lacking only the molluscum bodies, not yet formed, and again showing related pilosebaceous apparatus.

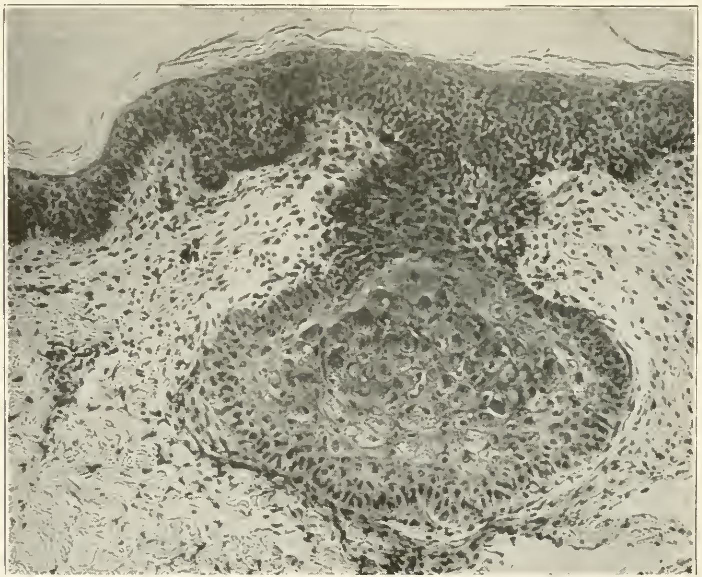


Fig. 14.—Well developed experimental lesion, eight weeks old with epithelial pedicle.

sections, and these, together with the study of many hundreds of sections not reproduced, have continually emphasized a relation with the glandular and follicular structures of the skin.

STUDY OF SIMILAR DISEASE IN ANIMALS

In spite of this experimental evidence, which is, without exception, in favor of the pilosebaceous origin of the disease, the opinion of those renowned investigators who believed otherwise, cannot be well ignored. Not entirely satisfied, therefore, an investigation of other experimental work suggested itself, with findings worthy of consideration. From time to time, experimental studies and observations have been carried out on a disease, clinically and pathologically identical with molluscum contagiosum of man, occurring in the lower animals.

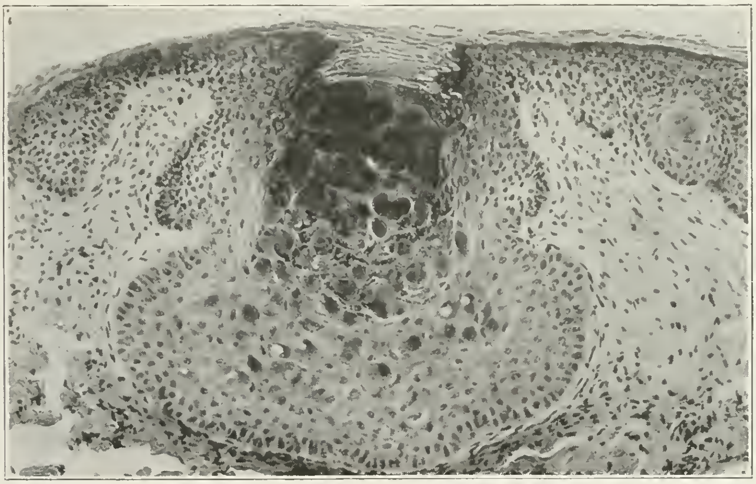


Fig. 15.—Adult lesion a few days older, presenting typical bodies, central umbilication.

As long ago as 1873, Bollinger[27] reported successful inoculations and transplantations in an investigation of the etiology of "Epithelioma Contagiosum" of domestic fowls. He was able to satisfy himself of the contagiousness of the condition, suggested as sites of predilection the comb, wattles, external ears, eyelids and feet of domestic fowls, and lastly he identified the histologic picture with that of molluscum contagiosum of man (Fig. 16). Hutchinson,[28] MacKenzie,[29] and

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[27] Bollinger: Ueber Epithelioma contagiosum beim Haushahn und die Sogenannten Pocken des Geglugels, Arch. f. path. Anat. u. Physiol. **58**:349, 1873.

[28] Hutchinson: Molluscum Contagiosum, etc., Clin. J. **5**:323, 1894-1895.

[29] MacKenzie: Molluscum Contagiosum in the Field Sparrow, Canadian Pract. & Rev. (Toronto) **26**:83, 1901.

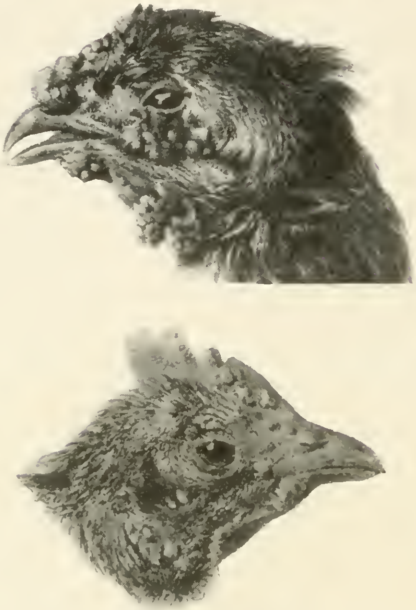

Fig. 16.—Lesions of "epithelioma contagiosum" occurring on combs, wattles, etc., of domestic fowl.

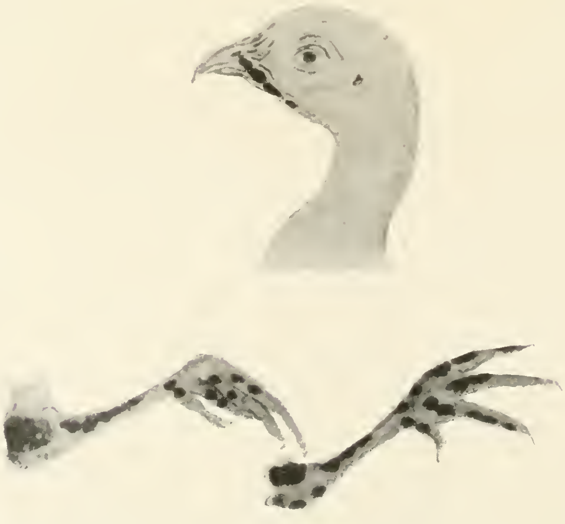

Fig. 17.—Case of "molluscum contagiosum" involving head and extremities of fowl reported by Fox.

Shattock,[30] a few years later, recorded individual observations of what they termed "molluscum contagiosum in both wild and domestic fowls." In 1898, Colcott Fox[31] presented to the Pathological Society of London, a case of "molluscum contagiosum" occurring in a young fowl (Fig. 17), and called attention to the identity of the clinical and pathologic picture, with that of molluscum contagiosum occurring in the human subject. And lastly, Marx and Sticker,[32] and Mariani,[33] have published the results of separate investigations of "Epithelioma Contagiosum of Fowls." The former were able to produce lesions histologically typical of molluscum contagiosum by rubbing the material from lesions of epithelioma contagiosum into the scarified combs of pigeons and chickens. Mariani points out in particular the similarity of the contagiosuness of the two conditions and the identity of the histologic pictures. The foregoing and numerous other references in the

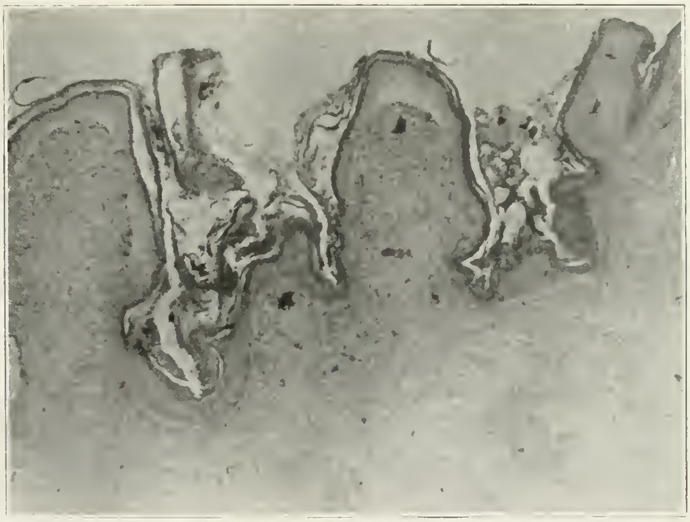

Fig. 18.—Section from comb of domestic fowl. Note absence of pilosebaceous structures.

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[30] Shattock: Molluscum Contagiosum in Two Bunting Sparrows, Trans. Path. Soc. London **49**:394, 1898.

[31] Fox, C.: Molluscum Contagiosum of Legs, Feet and Head of the Chicken, Trans. Path. Soc. London **49**:393, 1898.

[32] Marx and Sticker: Untersuchungen über das Epithelioma contagiosum des Geflugels, Deutsch. med. Wchnschr. **28**:893, 1902.

[33] Mariani: Beitrag zur Aetiologie und Pathologie des Molluscum Contagiosum des Menschen und des Epithelioma Contagiosum der Vogel, Arch. f. Protsitenkunde **21**:213, 1911.

literature leave no doubt that a disease, clinically and pathologically similar to molluscum contagiosum in man, occurs in the lower animals.

In not a few of the above studies certain sites of predilection were emphasized and an investigation of the comparative histology of these parts was undertaken (Figs. 18 and 19). A critical search of serial sections taken from the combs and feet of fowls has in no instance revealed the presence of sebaceous or other glandular structures, nor the suggestion of any analogue. It would seem that this is a point of extreme interest in the light of the interpretations of English investigators; Hutchinson, Fox, MacKenzie, and Shattock, each have reported their observations on what they have elected to term "molluscum contagiosum" in lower animals. Shattock, in particular, urges the identity of the two conditions, and gives as evidence, besides his microscopic findings, isolated cases of probable transmission of the disease from animals to man. For these investigators, the clinical and pathologic similarity, and the presumptive evidence of transmission, has warranted the use of identical nomenclature. Whether or not these two conditions are identical, as presumptive evidence would lead one to believe; or whether the virus causing these lesions has a certain specificity for the host invaded; are questions that must await the results of future investigations. For the present, one may go only so far as to say that the

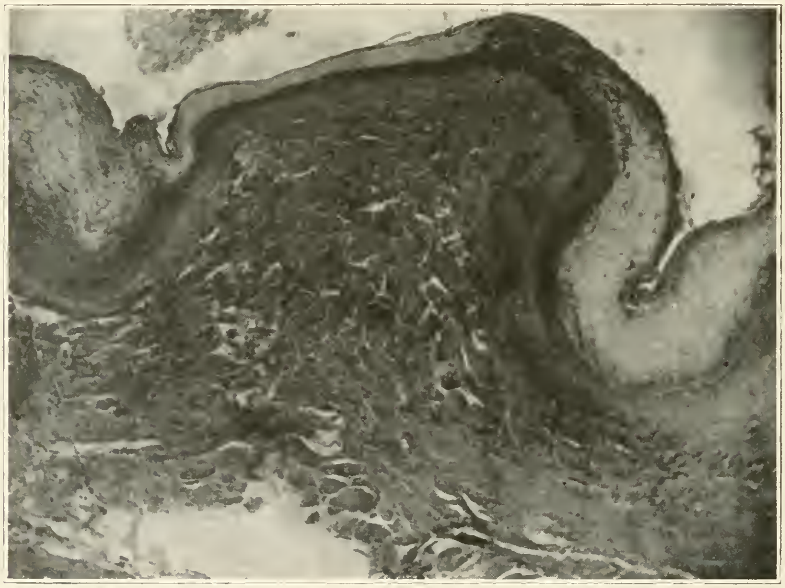

Fig. 19.—Section from leg of domestic fowl. Note absence of pilosebaceous structures.

analogue of molluscum contagiosum in man does occur in the lower animals, with clinical, pathologic and etiologic characteristics in common. Further, it may be said that the lesions of this disease are capable of developing independent of the pilosebaceous structures.

If we may consider the preexisting theories in the light of the present study, it would appear that each were correct in part. With sections exhibiting but one phase of development, or perhaps obtained from but one case, the reason is patent for previous views having limited themselves to a follicular or nonfollicular origin of the disease. Without doubt, certain cases or at least certain lesions present a pathology which exactly limits itself to the pilosebaceous apparatus. In addition, such a contention may be well supported by the lobulated outline often assumed, the clinical symptom of pruritus, and lastly the ease with which an etiologic agent might gain entrance through the follicular openings of the glaborous skin. To other investigators it may well be that only epithelial changes were evident. There were no glandular structures related in the sections studied and the usual tests for fat, when applied to the so-called molluscum bodies, were negative. If, however, one goes a step further, it may be recalled that embryologically the surface epithelium, the hair follicle and the sebaceous gland and duct have a common anlage. The outer layer of the embryo consists only of ectoderm, from which downward invagination, and subsequent proliferation, result in the pilosebaceous apparatus of the adult, while from the surface portion develops the cutaneous envelope. Embryonically, and we may almost say potentially, therefore, these structures are similar, and given favorable soil, i. e., susceptible individuals, it is but reasonable to believe that the same causative factor may result in changes pathologically similar, whether it be implanted one place or the other.

CONCLUSIONS

1. Studies by Wile and Kingery have shown the development of experimental lesions of molluscum contagiosum to be limited to pilosebaceous epithelium.

2. An abundance of clinical and pathologic evidence favors the existence of the analogue of molluscum contagiosum in fowls.

3. Absence of pilosebaceous epithelium in the combs and feet of fowls and pigeons, where lesions of molluscum epitheliale often occur, justifies the conclusion that the lesions of this disease can develop independent of pilosebaceous structures.

4. Presumptive evidence points to the identity of molluscum contagiosum in man and molluscum epitheliale in lower animals. Final proof of the development of molluscum contagiosum from the surface

epithelium, therefore, must depend on the establishment of the identity of these two conditions. This identity will be proved only by the successful inoculation of molluscum contagiosum into fowls, and of molluscum epitheliale into human subjects.

5. Experiments directed toward this end have been undertaken in this laboratory.

For the privilege of undertaking this work and for constant and invaluable advice during its completion, I wish to express my indebtedness to Prof. Udo J. Wile.

ABSTRACT OF DISCUSSION

Dr. J. M. King, Nashville, Tenn.: In 1904 Dr. Crocker of London received a parrot from South America. The bird had papules all over the body, neck and head. The case was diagnosed by Dr. Crocker and Dr. Pernet as molluscum contagiosum. I do not know what the laboratory reported.

Dr. Walter J. Highman, New York: I was taught that molluscum starts in the malpighian rete. The relation of the growth to the pilosebaceous glands is clearly brought out in Dr. Kingery's paper and is quite at variance with the older ideas. Is the disease found in fowls known as "pigeon epithelioma"? Prowazek thought he had found the cause of pigeon epithelioma and he considered the disease closely allied to molluscum contagiosum in man.

Dr. Lyle B. Kingery, Ann Arbor, Mich.: So far as I know, while the investigators believed the disease to be of parasitic origin, they were unable to cultivate or demonstrate a specific organism.

PROLONGED ICE BOX VERSUS SHORT WATER BATH INCUBATION IN WASSERMANN REACTION *

WARD BURDICK, M.D.
DENVER

The Wassermann reaction is one of the most widely practiced laboratory tests, in spite of its technical shortcomings. It has passed through many stages of evolution, undergone many refinements of technic from time to time, suffered many attempts at its modification, and been lauded and maligned, but it still stands as a monumental aid in the diagnosis, treatment and prognosis of syphilis; however, any further refinement that will increase its efficiency is obviously desirable. The conventional practice of the half hour primary incubation is the phase which I shall call into question at this time, as I believe it to be entirely inadequate and at the bottom of many of the discrepancies between the laboratory and the clinical findings.

The fixation of complement by syphilitic antibody or reagin depends primarily on three factors, namely, the amount of reagin in the quantity of serum, usually 0.1 c.c., the degree of dilution of the serum, and the time allowed for the reaction to take place. Given a serum with a large reagin content and a low dilution, that is, only that degree of dilution which would be brought about by the addition of the other elements of the test, namely, antigen and complement first, and then amboceptor and cells, fixation is instantaneous and requires no primary incubation. If the same serum is diluted, it will be found that the velocity of fixation is in inverse proportion to the degree of dilution.

Now, since the reagin content of serums to be tested in routine Wassermann work is an unknown quantity, and since the routine dilution practiced by many serologists using the original Wassermann system is that involved in bringing the whole up to 2.5 c.c., it follows that the only chance of injecting flexibility into the reaction is in alteration of the time of primary incubation. It is obvious that syphilitic serums with a small reagin content, such as are found in the early, primary and the late tertiary stages of the disease, may, and often do, yield faintly positive or entirely negative results when allotted only thirty minutes' primary incubation in the water bath.

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* Read before the Section on Pathology and Physiology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

* From the Research Laboratory, National Jewish Hospital for Consumptives.

To determine the effect of prolonged primary incubation, a series of Wassermann reactions was examined, both short (one-half hour) and long (twelve hour) periods of primary incubation being employed, and otherwise exactly the same technic to both sets of tests being applied.

Since complement is thermolabile, it is obvious that long periods of incubation cannot be carried out in the water bath, but must be done at low degrees of temperature. The average laboratory refrigerator will maintain a temperature of from 4 to 8 C., while it has been shown that 0 C. gives the best results; my experiments have been carried out at about 6 C., the temperature which the average serologist will find convenient.

TECHNIC

In the antisheep hemolytic system the native antisheep amboceptor was removed from all serums found to contain it. Each test was performed with five antigens: cholesterinized alcoholic extract of human heart; cholesterinized alcoholic extract of guinea-pig heart; plain alcoholic extract of human heart; plain alcoholic extract of guinea-pig heart, and acetone insoluble lipoids of human heart. Amboceptor titration was performed for each test separately, 0.1 c.c. of the serum to be tested being added to each titration tube. Two units of amboceptor were used in the tests. Complement was pooled from three or more pigs and was used in fixed amount (0.5 c.c., 1:10 dilution); 0.5 c.c. of 2.5 per cent. washed sheep cells; all tubes were brought up to 2.5 c.c. with physiologic sodium chlorid solution. Amboceptor titration tubes for the ice box reactions were set up with the test, with omission of amboceptor and cells which were added and incubated in water bath one-half hour prior to secondary incubation of the test. It was found that the ice box tests usually required one more unit of amboceptor than the water bath.

The results are given in Table 1.

TABLE 1.—Comparison of the Prolonged Ice Box and Short Water Bath Incubation Periods

	Non-syphilitic	Second Stage		Third Stage	
		Untreated	Treated	Untreated	Treated
Total number cases	72	8	20	18	49
Total number positive	0	8	10	18	43
Total number negative	72	0	10	0	6
Positive with both methods	0	8	3	10	18
Negative in water bath, positive in ice box	0	0	7	8	25
Per cent. total positive	...	100	50	100	87.7
Per cent. total negative	100	...	50	...	12.3
Per cent. positive in water bath	...	100	15	55	36.7
Per cent. positive in ice box	...	100	50	100	87

COMMENT

In this series, unfortunately, there are no primary cases. Of the 167 serums reported, seventy-two were from nonsyphilitic individuals so far as could be determined by history and diagnostic methods;

twenty-eight were from frank secondary cases and sixty-seven from long standing cases, most of which presented positive spinal fluid findings. It will be seen that 100 per cent. of the nonsyphilitic serums gave negative results by both methods. All of the untreated secondary cases yielded positive Wassermann reactions by both methods, while those of this class, both sufficiently and insufficiently treated, showed 15 per cent. positive by the water bath method as against 50 per cent. ice box. This indicates that a large percentage of second stage syphilitics are sent away with a verdict of cured on the strength of the old method Wassermann test, when in fact a longer primary incubation period, of twelve hours of these serums at ice box temperature, would reveal many of them positive and prevent the serious consequence of premature dismissal of such a patient. It is a grave error to advise a third stage suspect that he or she is nonsyphilitic on the strength of a negative Wassermann, when such a serum has been allowed only one-half hour for fixation of complement at water bath temperature. Results on this series of third stage untreated serums reveals this fallacy. This series reveals the discrepancy as entirely technical and in no wise real. Of the eighteen untreated third stage serums, thirteen were from tabetic patients, 100 per cent. of which yielded frankly positive Wassermann reactions by the ice box method of incubation.

As to the serums from the third stage cases under treatment, it will be seen that much the same ratio exists between short and long period incubation results. It is true that the series is not large; but the results are striking and the subject of sufficient interest to warrant this report in the hope that other serologists will extend this study.

A series of spinal fluids from patients with cerebrospinal syphilids were titrated by both methods, with plain alcoholic extract of human heart as antigen. These tests revealed that a positive result is frequently obtained by the prolonged ice box incubation, whereas a negative result is obtained by the conventional water bath incubation period. A typical case is illustrated in Table 2.

TABLE 2.—Wassermann Reaction on Spinal Fluid of a Patient with Tabes, Incubated by Both Methods

	Patient R. B. K., Tabes Dorsalis, July 6, 1919	
Quantity of Fluid Used	Water Bath Method ½ Hour Incubation	Ice Box Method 12 Hour Incubation
0.05	0	0
0.1	0	0
0.2	0	++++
0.4	0	++++
0.6	0	++++
0.8	0	++++
1.0	++	++++
1.5	+++	++++
2.0	++++	++++

SUMMARY

In the determination of syphilis by means of the Wassermann reaction prolonged, twelve hours, primary ice box incubation possesses decided advantages over the short period, one-half hour, incubator or water bath treatment. Serums giving doubtful reactions by the later method of primary incubation frequently are frankly positive by the former method. In the series studied both methods gave uniformly negative results in 100 per cent. of the clinically nonsyphilitic cases, and positive results in 100 per cent. of the second stage untreated cases. In the second stage treated cases, however, there was a decided difference, especially in the higher percentage positives obtained by the prolonged primary ice box incubation method. Likewise this method gave a decidedly higher percentage of positives in the third stage untreated (attaining 100 per cent. as compared to 55 per cent. by the half-hour water bath method) and the third stage treated cases. In the examination of spinal fluids from patients with cerebrospinal syphilis there frequently is obtained a positive reaction by the prolonged ice box incubation, whereas the conventional water bath method may be negative.

Metropolitan Building.

ABSTRACT OF DISCUSSION

Dr. John A. Kolmer, Philadelphia: In our studies of the last four years on the standardization of the Wassermann test, we found that primary incubation has required a large amount of work to reach a decision. Our conclusion, based on comparative tests conducted with seventeen different methods of primary incubation, is in favor of the refrigerator method. Our work was conducted with three different kinds of antigens, namely, cholesterinized extracts, plain extracts and extracts of acetone insoluble lipoids. In our experience, from sixteen to eighteen hours at 8 C. results in stronger reactions with all antigens than one hour in the water bath. As to the reasons for these stronger reactions: Our studies have disclosed that complement itself deteriorates to a greater degree in the refrigerator after eighteen hours than in a water bath for one hour. Also more complement is absorbed by antigen alone and serum alone in the refrigerator than in the water bath. Both of these nonspecific factors cause a closer adjustment of the hemolytic system, but there is, also, a greater fixation of complement by mixtures of serum and antigen after eighteen hours at 18 C. than after one hour at 38 C. in either water bath or incubator. Complement fixation tests conducted with the technic of Browning and McKenzie, by which the amount of complement absorbed by serum alone, antigen alone and mixtures of serum and antigen are measured, have shown that more complement is absorbed by mixtures of serum and antigen in the refrigerator at 8 C. than for one hour at 38 C. It is very important, however, to have the hemolytic system suit the method in order to avoid nonspecific reactions. What may be a satisfactory method for the water bath may not be satisfactory for the refrigerator method. A primary incubation of four hours at 8 C., plus one hour in the water bath, gives admirable results; but it may crowd the day, hence it is better practice to spread the work over two days and conduct the primary incubation for from sixteen to eighteen hours at 8 C. Dr. Burdick, have you compared this refrigerator method with the method you described for testing active serum?

Dr. C. C. Bass, New Orleans: I have been impressed with the fundamental fact that the degree of concentration determines very largely the velocity of antibody reactions. Agglutination reactions may take place in a very short time if fairly concentrated antigen and sufficiently concentrated serum are used. I have not been able to ascertain the optimum primary incubation period in complement binding reactions. I think that any complement binding antisyphilitic serum will bind as much complement in five minutes when there is enough concentration, as it will in much longer time when there is a greater dilution. The same is true in regard to temperature. If the temperature is high, the reaction is rapid. If the temperature is low, the reaction is slower. I have not been able to convince myself that there is the slightest gain in making the Wassermann test by long incubation with greater dilution, over shorter incubation with lower dilution. My own experience has shown that concentrated solutions or concentrated tests in short periods are as dependable as the opposite.

Dr. Ward T. Burdick, Denver: Answering Dr. Kolmer's question, I have not applied the ice box technic to the raw serum method. The method described is of particular importance in the third stage of syphilis. It is very distressing to have a patient, whose physical examination points clearly to syphilis, sent to the laboratory for a Wassermann test and be compelled to return a negative report, as is so often the case. In these cases we have simply not given the reaction sufficient time to take place.

MALIGNANT DEGENERATION IN BENIGN DERMATOSES *

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NEW YORK

The development of malignant neoplasms on dermatoses of the most varied sorts, often of many years' duration, is an occurrence too familiar to all dermatologists to admit of discussion; but to form a just estimate of the dermatoses in which such development is most frequent, to determine the proportion in each class which will probably become malignant, to ascertain the causes which lead to such degeneration — these are more difficult problems and, for the moment at least, insoluble. They are so important, however, especially as our attitude toward them must determine our treatment of many of the so-called precancerous conditions, that an attempt to formulate our present knowledge may be useful.

PRECANCEROUS DERMATOSES

Naevi.—The naevi come first to mind, and it is about the naevi that most has been written in this connection. The vascular naevi may be dismissed at once as no assertion has been made that they are especially prone to malignant degeneration. The case in regard to pigmented naevi is entirely different. There is no questioning the fact that some of these become cancerous, but opinions as to the probability of this occurrence show the greatest divergence. Bloodgood [1] says: "The mole which had become malignant was never a flat pigmented area not elevated above the epidermis, but was distinctly a projecting tumor. It is my opinion that all such moles should be removed, especially when they are in localitites exposed to trauma. Pigmented spots are entirely different." Pusey,[2] on the other hand, says: "The especially dangerous mole is the blue or black mole, which may be slightly elevated or which may, on the other hand, be embedded in the skin and show through only as a bluish black or coal black spot. Malignant degeneration is a very real danger in moles, but so much attention has been given to the possibility lately that the danger of their becoming malignant is, I believe, commonly exaggerated. Malignant growths beginning in moles frequently occur, but when one remembers that hardly an individual lives who has no moles, the relative infrequency of their degeneration becomes evident." Highman[3] even goes so far as to state that "it appears justifiable to eliminate birthmarks from the precancerous dermatoses." There are all shades of differences between these extremes. The general tendency is for the surgeons, who see cases of naevocarcinoma which have become a serious menace to life or even fatal, to incriminate all naevi; while the dermatologists, who see thousands of naevi that remain benign to one that becomes malignant, are naturally more conservative. Pusey's statement is probably nearer the truth than Highman's. We have no statistics to show the proportion of moles that become malignant, no extensive and accurate statistics to show the proportion of cases of cancer which have developed from moles; and even if we had them, these data would not be enough to enable us to solve the problem.

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

[1] Bloodgood, J. C.: The Surgical Treatment of Cutaneous Malignant Growths, J. A. M. A. **55**:1615 (Nov. 15) 1910.

[2] Pusey, W. A.: Principles and Practice of Dermatology, Ed. 3, New York, D. Appleton & Co., p. 896.

Let us assume, for the sake of argument, that under similar conditions normal skin and naevi have the same tendency to undergo malignant degeneration. If this were true, then on any part of the body — the face, for example — the cancers developing from normal skin should exceed those developing from naevi in the same ratio that the area of normal skin on the face exceeds the area covered by naevi. In that case, the cancers arising on naevi would be a small proportion of the whole, whereas we know that they form a large proportion. Wilson and Kalteyer[4] collected the reports of fifty cases of so-called sarcoma of the skin and found that in 69 per cent. the primary growth had its origin in a mole or naevus, and in some of these traumatism of the mole seemed to act as an exciting cause. They quote Eve's report on melanosarcoma in the London Hospital, who found that of thirty-three cases occurring in the skin, twenty-six began in pigmented moles, and that in a few cases a history of irritation by scratching was obtained. There seems to be no doubt, therefore, that a pigmented mole is more apt than is normal skin to furnish the starting point of this particularly malignant growth; but the danger must be slight, since practically every person has at least one mole, as any surgeon who examined the drafted troops two years ago can testify.

Nearly every observer states that in many or most cases it was possible to obtain a history of repeated slight traumatism before the development of the cancer. It would seem to be reasonable, therefore, to remove all moles which are subject to traumatism — as by the friction of clothes — and to leave the others until they show signs of change by increase of size or by subjective feelings of itching and pricking which would lead to scratching, when operation should be immediate. In practically all cases, the traumatism which seems to lead to malignant change is slight but continuous or at least frequently repeated. A single injury is generally without result. It follows from this that there is no objection to removing a mole by electrolysis or by freezing instead of resorting to operation.

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[3] Highman: Precancerous Dermatoses, J. Cancer Res. **1**:343, 1916.

[4] Wilson and Kalteyer: Sarcomatosis Cutis. Am. J. Med. Sc. **126**:757 (Nov.) 1903.

Recklinghausen's Disease.—This is so uncommon that it is clinically of little importance. Garré[5] estimates that 12 per cent. of the cases become sarcomatous, and many such cases are recorded. His estimate is probably grossly exaggerated, as it is based on seventeen cases of sarcoma developing in the 150 recorded cases of the disease. The assumption that the 150 recorded cases are any just measure of the prevalence of Recklinghausen's disease is manifestly absurd.

Xeroderma Pigmentosum.—The tendency of xeroderma to develop into carcinoma is too well known to require comment. The occurrence of the disease on the exposed parts brings the malignant change in line with the development of keratoses and finally of epithelioma in the skin of persons much exposed to the actinic rays of the sun.

Senile Keratoma.—Of the various acquired dermatoses furnishing a starting point for cancer, the most important is undoubtedly the senile keratoma. I have never been able to convince myself that there is any essential difference between this lesion and the seborrheic wart; the "sailor's skin" of Unna belongs in the same class. Here we encounter the same difficulties that beset us in considering the naevi — a multitude of reports of epithelioma which have developed from a keratomatous base, and a great paucity of statistics to show what percentage of these lesions undergo malignant change. The only estimate that I have seen is Hazen's[6] guess that "nearly 5 per cent. of all these keratoses terminate in cancer." He does not state whether he means 5 per cent. of the individual lesions or 5 per cent. of the persons affected — probably the latter — but in view of the extreme frequency of these lesions either estimate seems to me to be exaggerated. Nevertheless, the sequence is so frequent as to be noteworthy, and if any dermatosis deserves the name of "precancerous" it would appear to be this.

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[5] Garré: Ueber sekundäre maligne Neurome, Beitr. z. klin. Chir. **9**:465, 1892.

[6] Hazen: Skin Cancer, St. Louis, The C. V. Mosby Co., p. 35.

Hyde's[7] articles "On the Influence of Light in the Production of Cancer of the Skin," and McCoy's[8] on "The Solar Keratoses and Cutaneous Cancer" are interesting in this connection. McCoy insists, and justly, on the influence of the actinic rays in producing keratoses, and apparently most of the cases of epithelioma which he had treated had their origin in such apparently benign growths. Sutton's[9] paper on "The Symptomatology and Treatment of Seborrhoeic Keratoses" is most instructive, and in the main points is in accord with the others.

If it be granted that the number of epitheliomas developing on a keratosis is out of all proportion to those arising on normal skin, to what peculiarity of the altered skin are we to assign this susceptibility? It is easy to say that a continuation of the action of the actinic rays which produced the keratosis is sufficient to produce the cancer but, curiously enough, the keratoses are darker than the surrounding skin and are often covered by a crust; they should therefore be better protected against light than the rest of the epidermis, and if the actinic rays are the immediate cause of cancer we should see cancer developing from apparently normal skin rather than from keratoses. It seems probable, therefore, that the actinic rays produce a keratosis and that some other agent induces malignant degeneration. We are still ignorant of what this agent may be.

Leukoplakia.—Leukoplakia seems to be closely related to the senile keratomas of the exposed surface, and is due, in most cases, to an irritant acting over a long period of time — such as tobacco or the poison of syphilis. It is a well recognized precursor of cancer, or perhaps it would be more correct to say that most cases of cancer of the mouth develop on the site of a preexisting leukoplakia. The distinction is really important, for cancer of the mouth is rare in comparison with the great frequency of leukoplakia.

Cutaneous Horns.—Cutaneous horns form another group of conditions closely related to the seborrheal keratomas from which cancer may arise, but we have no statistics that give any hint of the frequency of this change.

Syphilis and Tuberculosis.—Of the various inflammations, syphilis and tuberculosis are probably those which most frequently lead to malignant degeneration. It is in the tongue that syphilis is most apt to be a precursor of cancer, and its influence is probably exerted by first causing ulceration or scar tissue, as in the scar of healed gummas

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7. Hyde: On the Influence of Light in the Production of Cancer of the Skin, Am. J. Med. Sc. **131**:1 (Jan.) 1906.

8. McCoy: The Solar Keratoses and Cutaneous Cancer, Arch. Dermat. & Syph. **1**:175 (Feb.) 1920.

9. Sutton, R. L.: The Symptomatology and Treatment of Seborrheic Keratoses, J. A. M. A. **64**:403 (Jan. 30) 1915.

or in the leukoplakias already mentioned. Butlin's[10] statement that "syphilis, in so far as it is capable of producing ulcers and scars of the tongue, so far is it capable of predisposing the tongue to the occurrence of carcinoma" is probably correct. Syphilitic ulcers and scars on other parts of the body do not seem prone to malignant change.

Tuberculosis, in the form of lupus vulgaris, is often mentioned as a possible precancerous condition, but here again it is not the lupus nodule that seems to be the point of origin, but rather the old chronic ulcer. During the past winter I saw a patient at the New York Skin and Cancer Hospital with an ulcerative lupus vulgaris of many years' standing, presenting a large epithelioma growing from a scarred and ulcerated area on the back of the neck, and also a small recent epithelioma developing on a senile keratosis on the right cheek, at some distance from any lupus tissue. I am not aware that this coincidence has been noted before. It suggests the possibility that the unknown cause of cancer — whatever it may be — found in this patient two regions prepared for its action by two separate and distinct causes.

Lupus Erythematosus.—This is a much less frequent forerunner of cancer than is lupus vulgaris. In ten cases in which I find the sequence recorded, it was always in the scar tissue that the degeneration began.

Ulcers.—Large open ulcers, like those caused by varicose veins, do not often develop into epitheliomas. Lynch[11] has recorded two cases of pellagrous ulcers, sections of which were shown by the microscope to be epithelioma, although the diagnosis could not be made by clinical examination.

Roentgen-Ray Burns.—The development of epitheliomas on old roentgen-ray burns is familiar; here again we encounter the familiar sequence — repeated irritation, atrophy, scar tissue, epithelioma.

CHEMICAL AGENTS PRODUCING CANCER

Among chemical agents with a reputation for producing cancer, two stand preeminent — arsenic and tar, the one acting apparently from within, the other from without; and in each case the development of cancer is preceded by the formation of a keratosis. The problem seems to be reduced, therefore, to the same terms as in the case of senile keratoma: Why and when does a warty growth become cancerous?

In this connection two articles in the *Journal of Cancer Research* for 1918 are most interesting. The first is by Yamagiwa and Ichikawa.[12] The investigators conducted a long series of experiments, painting with coal tar the inner surface of the ear of the domestic rabbit, an organ in which spontaneous new growth had never been reported. The alteration in the skin produced by the tar varied from an atypical overgrowth of epithelium to tumors which had the clinical and histologic appearance of cancer. Three of the cases are worth quoting in a little more detail.

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[10] Butlin: Diseases of the Tongue, Ed. 2, 1900, p. 315.

[11] Lynch: Epithelioma Developing in a Skin Ulcer in Pellagra, J. Cancer Res. **2**:77 and 131. 1917.

In Case 4 of the series, on the two hundred and seventy-third day, the painting with tar was discontinued. At that time there was an ulcer 2.8 cm. in diameter, raised above the skin, with raised edges, resembling a rodent ulcer. A nodule had developed on the outer surface of the ear in a situation corresponding to this growth on the inner surface. The nodule continued to grow after the cessation of the painting with tar, spreading along the surface; the lymph nodes at the root of the ear began to swell, and the animal commenced to lose weight. It died on the three hundred and sixty-sixth day, ninety-five days after the last application of tar—greatly emaciated. The tumor was then twice as large as when the irritant was discontinued. Microscopic examination of a piece of the tumor removed on the two hundred and seventy-third day showed carcinoma in its early stage, while two lymph nodes at the root of the ear and one of the submaxillary nodes showed solid and cystic metastatic nodules, the former consisting of masses of cancer cells, while the walls of the latter were covered with a many-layered epithelium which in many places had formed epithelial pearls and was infiltrating the lymph sinus and the surrounding tissues. Case 6 of the series was similar. The irritant was discontinued on the three hundred and twenty-second day and the animal died on the three hundred and thirty-eighth day, extremely emaciated. The ulcerated tumor and two lymph nodes at the root of the ear had continued to enlarge after the last application of tar. The microscopic findings were similar to those in the preceding case, and the metastatic growth in the lymph nodes was found to be infiltrating the surrounding tissue.

Case 7 of the series is in some ways the most important of all. The irritant was discontinued on the two hundred and fifth day. On the two hundred and eighty-sixth day a diffusely irritated spot on the treated surface began to enlarge, and by the five hundredth day it had produced a cutaneous horn. An ulcer appeared at the base, and on the five hundred and twentieth day the horn fell off, leaving an ulcer with edges raised 0.5 cm. from the surrounding surface and with an even finely granulated base. The ulcer continued to increase in size, and on the five hundred and sixty-fifth day the lymph nodes at the root of the ear began to swell. A fragment removed for microscopic examination had all the characteristics of a rodent ulcer; the epithelium had infiltrated into the lymph vessels and veins and formed a thrombosis of carcinoma cells in them; it had penetrated the ear cartilage and had produced an ulcerated nodule on the outer surface of the ear.

The authors conclude that the repetition or continuation of chronic irritation may cause a precancerous alteration in epithelium previously normal, and that if the action be continued carcinoma may be the outcome even though no specific agent has been interpolated.

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[12] Yamagiwa and Ichikawa: Experimental Study of the Pathogenesis of Carcinoma, J. Cancer Res. **3**:1 (Jan.) 1918.

These results may have an entirely different interpretation, however. The repeated applications of tar produced keratosis, and after a time growths which seemed to be true carcinomas appeared; but it is noteworthy that in one case the first clinical evidence of epithelioma appeared about ten months after the discontinuance of the irritation. The tar was the cause of the keratosis; but the malignant degeneration of this keratosis could not be the result of the irritation by tar, as tar was no longer used; it appears rather as if the horn itself were the irritant which induced the change.

Ross,[13] in the same volume, has an article which attacks the problem from an entirely different angle. Studying the occurrence of occupational cancer, he finds that in nearly every case the irritant is chemical, not mechanical. Gritty coal dust does not cause cancer, while soft soot does. Soot, it is to be remembered, is not pure carbon, but contains tar, and tar oils also. The occupations, among the workers in which he finds cancer to prevail, involve exposure to tar, pitch, soot and certain grades of paraffin; kangri cancer he believes is caused by the product of imperfect combustion in the brazier, rather than by the heat; and he calls attention to the frequency of cancer in tissues irritated by tobacco and betel nut, and among farm laborers who frequently handle manure and who show, according to the Registrar-General's returns for 1890-1892, an incidence of eighty-four deaths from cancer as against fifty-one for all occupied males. Broders[14] also finds basal celled epithelium more frequent in farmers than in others. Among the workers in tar and tar products, the especial incidence of cancer is confined to those who handle certain grades of the substance. He points out that all these substances which seem to have a tendency to produce cancer are the products, or are derived from the products, of the death and decomposition of living matter. Examining these substances still further, he finds that they all contain certain compounds which he calls auxetics and which have the property, experimentally proved, of promoting cell division. The coal products which do not seem to produce cancer were found not to contain auxetics. In occupational cancer, therefore, the auxetics, the inducers of cell proliferation, the predisposing cause of cancer, are introduced from without; in senescence, they are produced within the body by the physiologic increase of cell death; in cancer following traumatism, they are produced by local cell injury. It is to be noted, however, that in all these cases of occupational cancer there is first the production of a keratosis, then a malignant degeneration; and evidence is still lacking to show that this final change is the result of the same chemical action as the former.

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[13] Ross, H. C.: Occupational Cancer, J. Cancer Res. **3**:321 (Oct.) 1918.

[14] Broders, A. C.: Basal-Cell Epithelioma, J. A. M. A. **72**:856 (March 22) 1919.

IRRITATION COMMON ETIOLOGIC FACTOR

In reviewing these various forerunners of cancer, there is one factor common to all, and that is irritation — usually repeated over a period of months or years. Irritation by chemicals, by actinic rays, by roentgen-rays, by germ action or germ products, all lead to epithelial hyperplasia, or it may be to atrophy and scarring, but the action seems to end there. The keratotic or sclerotic tissue, however produced, is then the starting point of a change of a different order, which we call malignant degeneration. Ribbert[15] states, in concluding his great work, "Das Karzinom des Menschen": "Carcinoma develops on the basis of a subepithelial inflammation caused by epithelial products which decrease the differentiation of the epithelial cells and permit their downgrowth." Although he lays greatest stress on the subepithelial change, he finds the exciting cause in an epithelial product. Apparently, this substance is produced by the altered epithelium of keratosis and of scar tissue more often than by normal epithelium, but we are still ignorant as to why certain keratoses should produce it while others do not. It may be that mechanical irritation will so alter the metabolism of their component cells as to lead to the production of this hypothetical substance, but we do not know.

SUMMARY

To sum up, there are many causes which lead to keratoses and scars, and keratoses and scars are more prone to malignant degeneration than is normal skin, but the number of keratoses and of scars is so enormous and the number of epitheliomas relatively so small that the danger in each individual case is slight indeed. Our aim should be prophylaxis—to prevent the formation of these precancerous conditions; to watch and protect them when they appear; to remove them when exposed to injury or when they show signs of changing their character. But to recommend the removal of every scar, every naevus, every keratoma, when every person has at least one of these blemishes, or to frighten the public with tales of the menace of such growths, is not justified by the facts.

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[15] Ribbert: Das Karzinom des Menschen, Bonn, 1911.

PRODUCTION OF TUMORS IN THE ABSENCE OF PARASITES *

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VARIETIES OF TUMORS IN PLANTS

There are many kinds of tumors in plants. These are due to a variety of causes which are principally living things—gall flies, plant lice, nematodes, fungi, myxomycetes and bacteria. Tumors may also be due to frost (Harvey), to mechanical irritation (Wolf) and, as I hope to convince you, to a lack of aëration and the resulting increase in acidity of the imperfectly aërated tissues. Clinically, if we may use such a term in speaking of plants, the tumors are either benign or malignant, sometimes grading from one into the other, as in crown gall. Morphologically, they are almost as diverse in appearance as the causes that produce them. Their general structure depends not only on the stimulus received from the parasite, but also on a variety of internal conditions peculiar to the host plant. In other words, the response of the plant varies not only according to the quantity and the quality of the stimulus received, but also according to the age of the plant, the parts attacked, the conditions of nutrition, and various unknown factors, which leads on the one hand to resistance and on the other to increased susceptitbility. The cells composing these tumors may be slow growing and nearly normal in size and orientation as in benign animal tumors, or the tumor may consist of a congeries of small, rapidly dividing, deep staining, disoriented, destructive, anaplastic cells, strongly suggestive of the malignant tumor cells of animals. Every tumor, of course, has its stroma, variable in amount.

What form the tumor takes depends partly on its location; but to a much greater extent on whether the parasites are few or many, whether they are imprisoned in small chambers, as in the case of gall-fly larvae, or are free to move about in the tissue, as in the case of nematodes and bacteria. In the first case, the tumor tissue although hyperplasial approximates the normal tissue in form and arrangement of its cells, because the physical-chemical stimulus always proceeds in the same general direction, i. e., from a central cavity in all direc-

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* Read before the Section on Dermatology and Syphilology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

tions toward the periphery; there is, therefore, nothing to lead to disturbed growth and disorientation of cells. On the contrary, in a nematode or bacterial tumor the organisms are able to move about more or less and the chemical-physical stimulus proceeds sometimes from one direction and sometimes from another, leading to a frequently changed direction of growth and to much disorientation of cells. All tumors, so far as they are due to parasites, must be assumed to be due to the chemical-physical action of the by-products of the metabolism of these parasites, just as most communicable diseases are due not to the parasites themselves, but to their toxins. In case of crown gall, therefore, I cannot be properly accused of abandoning my first position, because I have undertaken to show that the parasite acts through its excretions. Diverse as are the tumors of plants due to parasites, I believe that the fundamental chemical-physical phenomena underlying them are much alike, and that the differences we see, when these differences are not due wholly to varying tissue reactions, must result simply from variations in volume, and direction and continuity of the chemical-physical stimulus. This must be true also of the nonparasitic tumors, and eventually I hope to be able to formulate simple general laws applying to all of them.

EXPERIMENTAL TUMORS IN PLANTS

This paper relates to the experimental production of small benign tumors. It would be of no special interest if it had not grown out of crown-gall studies and did not appear to throw some light on the general phenomena of tumor formation. I have been experimentally interested in crown gall for fifteen years. For those who do not know what has been done, I summarize the leading discoveries made during this time:

In the Department of Agriculture a widely distributed, harmful plant tumor has been demonstrated to be due to a schizomycete. Although no bacteria are demonstrable in sections of this tumor, nevertheless, they are present in it and can be isolated from it by using the methods of the bacteriologist. By pure culture inoculations with the organism, the tumor can be reproduced at will and has been so reproduced hundreds of times. It may also be reproduced by grafting portions on suitable parts of healthy plants. This tumor possesses the power of continuous growth through several generations (Jensen). It is a hyperplasia which often grows rapidly. It contains few or many vessels, depending on whether the inoculated infected tissues are themselves feebly or highly vascular. Often it is imperfectly vascularized and decays early with the production of open wounds which proliferate from their edges. The tumor destroys by crushing or by invasion. It often develops invasive tumor strands on which are formed secondary tumors which show the structure of the primary tumor. If inoculations are made in the vicinity of groups of totipotent cells (root, shoot or flower rudiments), the tumor which develops is an embryoma, i. e., it is a rapidly developing, disoriented, anaplastic tissue containing dwarfed fragments of various organs having normal cell orientation, but not necessarily normal organ position—they may be upside down in the tumor. Such fragments may also come to the surface or be borne on the surface and grow for a time as dwarfed shoots or other organs which in turn may be invaded by the tumor tissues. Like cancer, if taken early, the tumor may be removed completely; but in later stages of growth it often returns after removal.

The parasite causing this tumor produces ammonia, aldehyd and various acids, and with these substances I have succeeded in causing small hyperplasias in the absence of the parasite; I therefore assume that it is the by-products of the parasite liberated in the tissues which stimulate the normal cells to become tumor cells. These by-products—ammonia, acetic acid, formic acid, etc.—act, I think, by causing cell precipitates which upset respiration and compel the affected cells to rearrange their protoplasm and divide at once or perish. We must suppose that these substances are given off by the bacteria continuously in minute quantities sufficient to stimulate the cells but not enough to kill them.

Following out my theory that disturbed cell respiration is at the bottom of tumor formation, I tried last year to find what results I could obtain in the absence of parasites by limiting the intake of air in various ways, and in each experiment I reached the same result—increased acidity of tissues and the production of small hyperplasias.

I first experimented on the flesh of potato tubers, cutting out rectangular blocks under sterile conditions and hermetically sealing them in test tubes, the blocks resting on wet cotton. The tissues, being alive, continued to absorb water and to respire and transpire. They formed a cork layer over their cut surface and under this layer, as respiration and transpiration became increasingly difficult owing to the saturation of the air and its limited oxygen content, hyperplasias developed, rupturing to the surface. Titrations showed an increased acidity of the tissues. Sometimes these blocks of raw potato flesh developed shoots and roots which soon showed results of asphyxiation and these also bore many small hyperplasias. The tumors themselves rarely developed roots or shoots. Some of the tubes were kept in the dark at room temperature, and others were exposed in bright light to hothouse temperature, but the results were the same. I have been able to obtain in this way only small tumors, since in my potato blocks in sealed tubes the food supply is limited and the air soon exhausted; but by placing the potato flesh under better growing conditions with occasional renewal of the air, I believe it might be possible to induce the tumors to grow for a considerable period and perhaps to double or treble the size of any I have yet obtained. All of the tubes contained an abundance of water and the air was always saturated.

I obtained the same results, however, from whole tubers lying either in a covered pasteboard box in dry air on my laboratory table, or exposed to the light on the same table in a large open jar. The tubers pushed sprouts, but owing to lack of water these could not develop organs of respiration and transpiration (that is, leaves), and they became much thickened and covered with numerous small hyperplasias, located under wide open stomata. The tissues developing these hyperplasias were gorged with sugar and starch, contained more oxidizing enzymes than normal, and on titration proved to be several times as acid as normal shoots and tubers. Here again I think imperfect respiration led to increased acidity of the tissues and to the development of the tumors.

In a third series of experiments I obtained numerous small tumors from green potato stems in active growth by suddenly destroying the leafy tops, i. e., the respiring and transpiring organs. This immediately stopped the upward movement of a large quantity of aërated water; oxygen hunger and acidity developed and hyperplasias resulted.

Finally, I have repeatedly obtained the same results on the stems of a variety of plants by blocking the lenticels, which are aërating organs (organs both of respiration and transpiration), with Squibb's liquid petrolatum, following the petrolatum experiments of Wisniewski and of Schilling. As soon as the exchange of gases is interfered with, viz., the intake of air and the movement of aërated water to the surface, tumors begin to form under these lenticels.

In crown gall and various other tumors due to parasites the parasite furnishes the acids and other stimuli as a direct result of its metabolism, but the small benign tumors I am describing are not the result of parasitism. The increased acidity probably results from the incomplete combustion of carbohydrates, i. e., from anaërobic cell-respiration due to poor circulation and imperfect aëration, which we know to be a peculiarity of tumors in general, since most of them are poorly vascularized and out of the general circulation.

If, for any reason, conditions such as I have outlined should occur in parts of the animal body, I should expect to see similar phenomena arise in such parts and, the nutrition being more abundant, the tumors might become large. But as most tumors in plants, and especially in the more destructive ones, are the direct result of parasitism, parasites should also be looked for as the cause of rapidly growing, malignant animal tumors. We are forced to the belief that they must be of parasitic origin unless we are to regard plants and animals as so unlike that no conclusions drawn from the one can be made to apply to the other. Modern biology opposes such an idea.[1] Those who are interested will find this subject treated in more detail with numerous illustrations in my textbook on "Bacterial Diseases of Plants." [2]

SUMMARY

I have produced hyperplasias (1) by the direct application of dilute acids and alkalies to susceptible plant tissues; (2) by the introduction into the tissues of certain foreign organisms (especially the crown gall bacterium which produces acids and alkali in flask cultures and probably also inside the cells as a result of its metabolism), and (3) I can now bring about the same results in the absence of parasites and their products by limiting the intake of oxygen, thus compelling the cells themselves to manufacture the stimulus which leads to the development of hyperplasias. I can conceive of this taking place only as the result of an anaërobic cell respiration acting on the youngest, most active cells of a tissue; but there must be always some oxygen of the air present, otherwise there will be complete asphyxiation of the tissues, as happened in my first experiments. Probably overgrowths due to freezing and to mechanical injuries will also be found to depend on local interference with cell respiration.

The most striking tumors are obtained by inoculatitng the crown gall organism, *Bacterium tumefaciens*. Some of these are simple tumors and others are tumors containing roots and shoots. Some also show the beginning of secondary tumors, and in the embryomas the invasion of tumor tissue into the embryomatous parts (young roots and shoots).

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[1] Smith, E. F.: Crown Gall of Plants and Cancer, Science **43**:348 (June 23) 1916.

[2] Smith, Erwin F.: Bacterial Diseases of Plants, Philadelphia, W. B. Saunders Company; in press.

ROENTGEN RAYS OR RADIUM COMBINED WITH EXCISION IN THE TREATMENT OF KELOIDS *

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Keloids or hypertrophied scars are difficult to treat and require much patience on the part of both patient and physician. So far as is known, the roentgen ray and radium are the only two agents which will arrest the disease or cause it to disappear. If these agents are used early when the scar begins to hypertrophy there will probably be no need of combining excision with the radiotherapeutic effect. It is because of the frequent neglect of hypertrophied or growing scars that it is necessary to call attention to these methods of treatment. If the general practitioner, the surgeon and the dermatologist are alert and apply skilfully the roentgen rays and radium to scars that are beginning to show hypertrophy, keloids will almost be eliminated from the field of medicine. It is true that in many instances slight wounds, especially in the colored race, lead to the formation of large keloids and often these cause so little inconvenience to the patient that they are liable to be neglected until they have reached a considerable size. Too often, however, the surgeon recognizes his helplessness and therefore neglects the condition, and the patient, fearing further deformity from treatment, neglects the condition entirely. If we make it more generally known that radium and the roentgen rays will prevent these growing scars and generally cause their disappearance, patients will be more liable to seek assistance. While keloids or hypertrophied scars occur more frequently in the colored race, they are by no means confined to the colored race, and most patients who have come to me for treatment of this condition have been white. The underlying constitutional cause of the formation of keloids I believe is not known, but the exciting causes are known to all the members of this section, and since the exciting cause cannot be prevented, we need give it no consideration; we shall deal only with the neglect of actual keloids. Usually the patient seeks relief because of deformity or for cosmetic reasons, but occasionally pain is a prominent symptom and brings the patient for treatment. In other cases the keloid may cause actual mechanical obstruction, as when they occur on the feet and interfere with the wearing of shoes.

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* Read before the Section on Dermatology and Syphilology at the Seventy-First Annual Meeting of the American Medical Association, New Orleans, April, 1920.

The roentgen rays have long been used in the treatment of keloids, not only by myself but by many others. MacKee has been especially prominent in calling attention to the value of this method of treatment. The early work was done, as most radiotherapy was done early, by fractional and indefinite doses. Even with this indefinite technic some brilliant results have been obtained. Even today with more definite technic, much skill and much keen judgment will be necessary to obtain the best results, for no two cases react in exactly the same way. Generally, the aim should be to produce a progressive atrophy without erythema or destructive effect on the skin or overlying epithelium. The technic will vary considerably with the size or thickness of the keloid, especially in the cases in which the roentgen rays alone are used. The thicker and older keloids will require more filtration and correspondingly longer treatment. In recent cases of hypertrophied scars, in which the scar tissue is still quite young, considerably less treatment and less filtration is necessary. In these mild types one can use to advantage 5 milliamperes of current, 2 millimeters of filter, with a focal distance of 8 inches, a parallel spark of 9 inches, for a period of two minutes. This will give approximately 8/10 of an erythema dose, and will be within safety limits. This treatment can be repeated in three or four weeks. It must be borne in mind that the factors given will vary in value considerably according to the instrument used, and

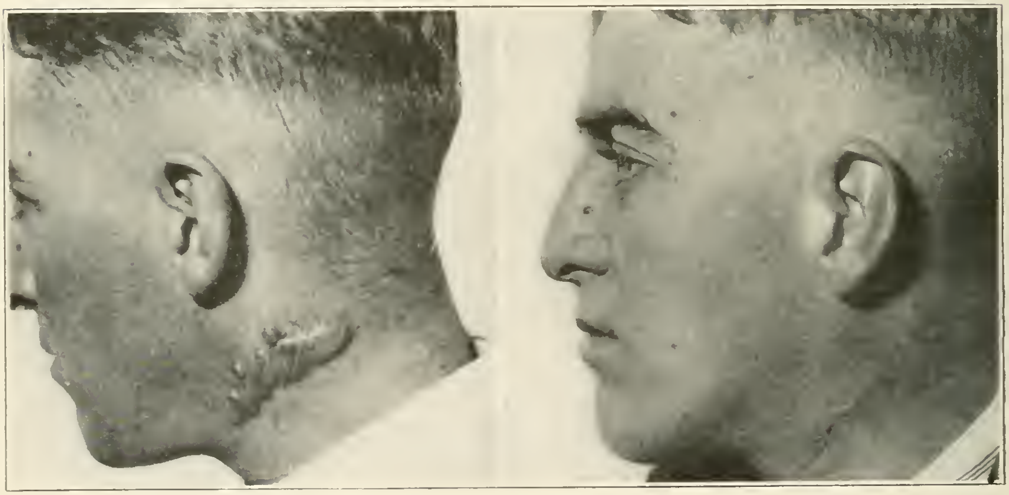

Fig. 1.—Appearance of patient Oct. 6, 1919, with a keloid following operation for an enlarged gland. He was given one full dose of roentgen rays Oct. 6, 1919, and excised within a few days. He was treated again with the roentgen rays Oct. 23, 1919; Nov. 29, 1919; Dec. 20, 1919; Jan. 17, 1920, and March 13, 1920. The second photograph was taken Jan. 17, 1920.

one must familiarize himself with the value of each particular instrument. In the thicker and older cases of keloid which one is trying to eliminate by the roentgen-ray treatment alone, it is desirable, when possible, to obtain a cross-firing effect. When this is possible, the area to be affected is divided into two or more portals of entry, and the rays so directed through these various fields that the deeper portions of the rays will cross in the deepest portion of the tumor. In these cases it is desirable to use the following technic: 5 milliamperes with 6 millimeters of filter, a focal distance of 8 inches, and a parallel spark of 9 inches for a period of eight minutes.

TREATMENT BY RADIUM

Radium will give very similar results if used in corresponding doses; that is, in the treatment of keloids one can produce results almost identical with those obtained from the use of the roentgen rays. Plaques or capsules may be used. One should learn the value of the particular specimen that is being used, and it should be used long enough to produce an erythema dose, with a filtration equal to approximately 0.5 mm. of silver. This will eliminate about 98 per cent. of the beta rays. The duration of treatment will vary according to the size of the specimen used and the size of the keloid which is to be treated. In order to use the radium skilfully, the value of the speci-

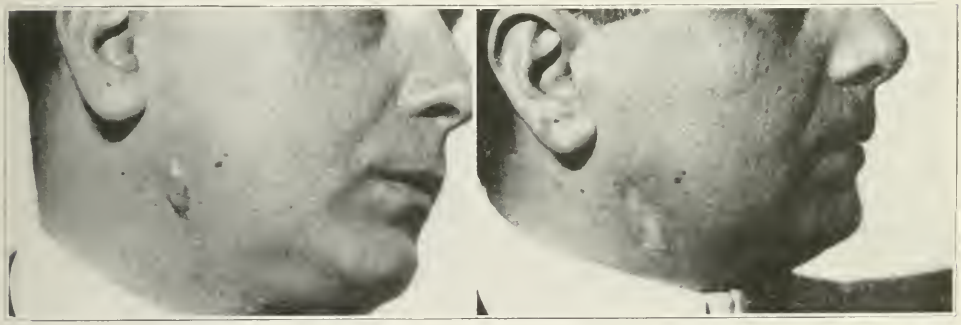

Fig. 2.—Appearance of a patient June 24, 1919, with a keloid following the pinching of a small papule. It had been burned out with acid but recurred. One dose of roentgen rays was applied June 24, 1919. The keloid was immediately excised and treated July 23, 1919, with 50 mg. of radium in 0.5 mm. of silver, and 2 mm. of rubber, applied one-half hour. Aug. 18, 1919, 100 mg. of radium were applied for one hour, filtered through 0.5 mm. of silver and 1 mm. of rubber. Sept. 29, 1919, 100 mg. of radium were applied for thirty-five minutes, filtered through a 0.5 mm. of silver, and 1 mm. of rubber. Nov. 11, 1919, 100 mg. of radium were applied for half an hour, filtered through 0.5 mm. of silver and 1 mm. of rubber. The second photograph shows his appearance March 22, 1920.

men over a given area with the filtration above mentioned at a given distance should be known. From this the necessary distance and area can be calculated according to well-known methods. A 50 mg. capsule in 0.5 mm. of silver and 1 mm. of rubber in direct contact will produce an erythema dose in one hour.

SURGERY COMBINED WITH RADIOTHERAPY

My chief object is to emphasize the value of this combination. It is not new, and is only original in the sense that I have arrived at the conclusion of the value of this treatment, and have been recommending it for a number of years independent of the knowledge that others have been doing likewise. MacKee[1] says in very large keloids it is preferable to ablate, and then apply the roentgen rays as prophylactic. This may be done also in small keloids in order to obtain a perfect cosmetic result. He also says:

> I have never observed a recurrence after roentgen-ray treatment. When one is treating a very large keloid so much radiation is necessary that there is danger of a degeneration or ulceration with secondary carcinoma formation. At any rate, in the very large keloids one often will fail to reduce them absolutely flat with the skin. Therefore, for cosmetic reasons alone it is advisable to excise and then treat.

The method that I have been recommending as a rather routine procedure is the application of the roentgen rays to the keloid area preceding the operation, preferably a few days to two weeks before, and of a dose such as one would give if the rays were to be depended on to remove the keloid. The keloid, or hypertrophied scar, is then carefully excised. This can be done best when there is sufficient loose tissue or skin round about to close the wound without too much stretching, and I believe that the surgeon should excise as nearly as possible to the outline of the keloid and not attempt to excise wide of the area. I have had surgeons unfortunately make a wide incision such as they would make when removing a malignant growth. This extensive excision only increases the area of scar tissue, for even though the keloid is excised, there will always be a scar. The advantage of excision and combined anteoperative and postoperative roentgenotherapy or radiotherapy consists in the reduction of the scar to the level of the skin, and in many instances of a decrease in the total area of the scar. I usually advise a full dose of roentgen rays within a week or ten days after the excision of the scar. The patient is then seen weekly, and if there is any tendency toward recurrence, more treatment must be given. Three or four applications of the rays should be given to guard

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[1] The Roentgen-Ray Treatment of Skin Diseases, J. A. M. A. **65**:1886 (Nov. 27) 1915.

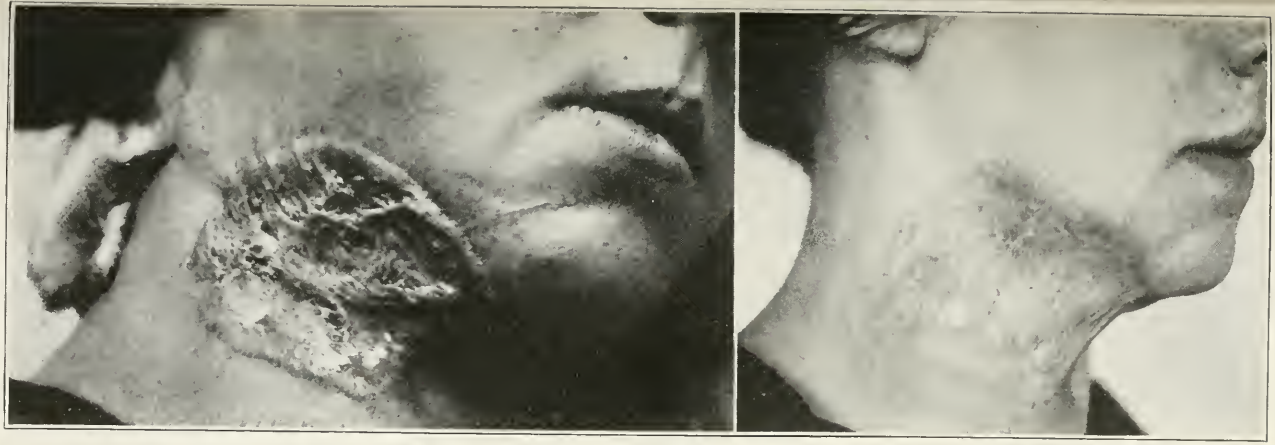

Fig. 3.—Appearance of patient Jan. 21, 1913, who developed a keloid following a burn when a child. Fourteen fractional doses of roentgen-ray treatment were given between Jan. 21, 1913, and Dec. 22, 1913, each application measuring about half of a skin dose. The second photograph shows her appearance Sept. 9, 1916. The scar is soft and healthy.

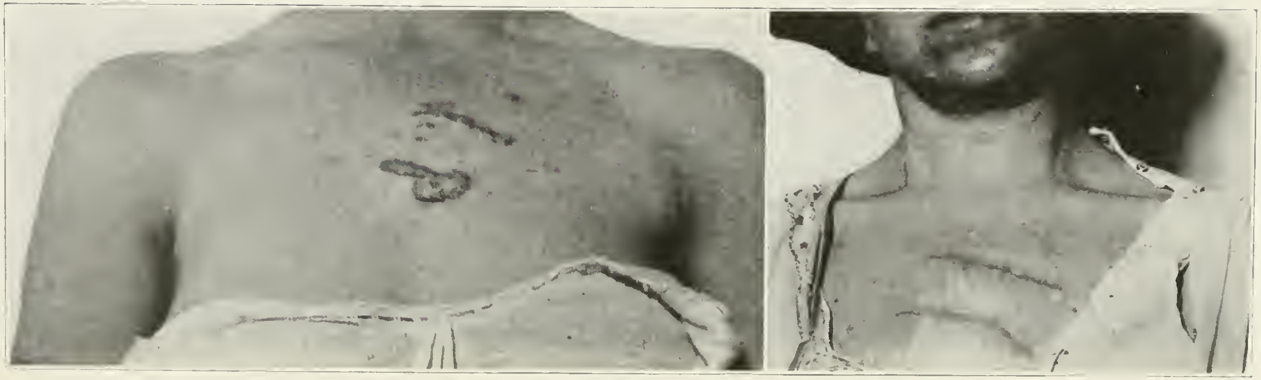

Fig. 4.—Keloid following sunburn; it was treated with the roentgen ray, excised and again given roentgen-ray treatment.

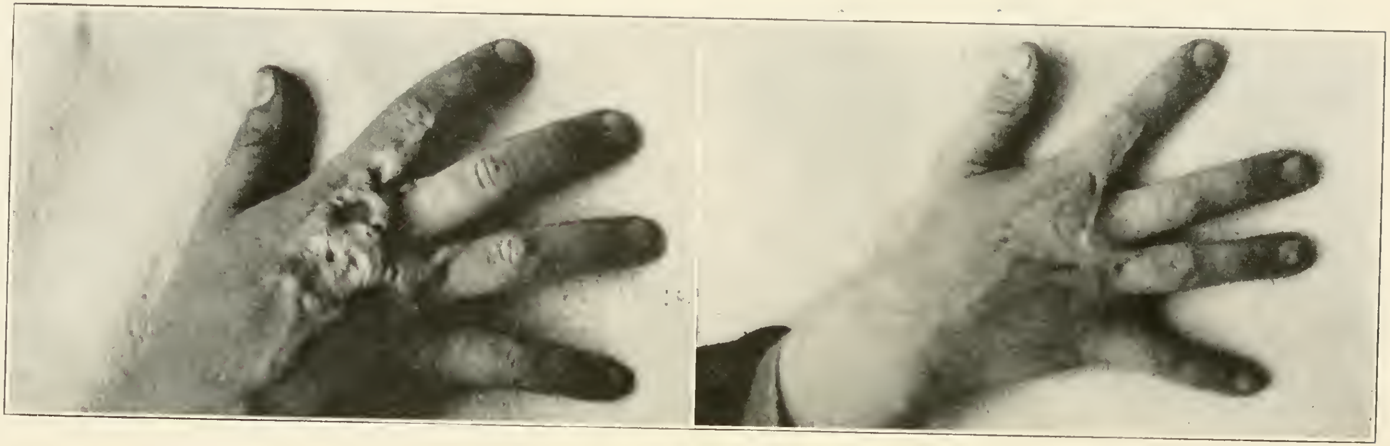

Fig. 5.—Keloid following a burn; treated with nine fractional doses of roentgen rays.

more certainly against a recurrence of the keloid. In several of my cases there has been a tendency toward recurrence following this excision, but in every instance it was thoroughly controlled by either the roentgen rays or radium. In some instances, in which there was localized thickening in the scar, I seemed to get more benefit from the local application of the radium, and this effect seemed to be slightly more positive than when I depended on the roentgen rays.

CONCLUSIONS

1. Keloids should be treated by radiotherapy as early as the hypertrophy of the scar can be recognized.
2. Radiotherapy can be depended on — either the roentgen rays or radium — for the reduction of a keloid.
3. The best results will generally be obtained when radiotherapy is combined with excision. If applied before and thoroughly after excision, a flat, soft, smooth and inconspicuous scar should be found.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. WILLIAMS, SMITH AND PFAHLER

Dr. Norman Walker, Edinburgh, Scotland: Malignant diseases of the skin have a practical importance in connection with certain industrial processes in our country. The Home Office recently requested that I investigate the distribution of malignant growths in the skin in connection with shale workers. I used to see a bad case occasionally in my time, but I had no idea that the condition was so widespread as it turned out to be. The shale industry gives employment to several thousand men and I had an opportunity of inspecting many of them. Much light may be thrown on the possible cause of these cancers by the investigation of industries. It did not take much investigation to find that we go far too wide when we talk of tar, pitch and paraffin as the causes of these growths. It is possible to pick out the particular kind of work that produces them. The men know this very well. The "green sheds" are the ones that produce these disorders, and wise men refuse to work there, for a large percentage of men working there are afflicted. Men who have worked for twenty-five years may show no irritation. It takes from three to five years to show any irritation, and usually it is seven or eight years before malignancy develops. These growths are of the type of senile keratoses and the patients, as a rule, do not see the doctor about them. They have learned that the application of crude hydrochloric acid is sufficient to cure them. The men who have worked in shale for a number of years are scarred all over with the lesions they have removed. In some instances the growths spread to the glands and kill the patient. The interesting point is that in this particular industry the lesions are limited to the arms and legs, which are exposed. All sorts of precautions are resorted to by the men. If they smear their arms with castor oil before going in, the risk of irritation is greatly decreased. I also inspected the briquet industry in Cardiff, where they mix coal dust with pitch. A great many of the workers had growths, but they were not at all like the paraffin growths. They were found occasionally on the hands and on the scrotum. The most remarkable finding was their presence on the neck. Further, most of them presented a remarkable sensitiveness to light. One man told me that he felt so much agony on a sunny day that on sunny holidays he retired to his coal cellar where it was perfectly dark, in order to get relief from the pain. About three months ago a man walked into my clinic with a malignant tumor on his hand and other keratotic lesions. He was employed in mending fishing nets. There were only four lesions and two had cancers caused from the tar which was used on the material in the nets. There are three types, the tar, the pitch and the oil cases. These cases are evidently due to certain peculiarities in the skin of the person. About 25 per cent. of the men in the green sheds were affected, a much smaller percentage of the pitch workers and a much larger percentage of the tar workers. A Belgian doctor told me that in the Brussels briquet works during the war there was a great deal of carcinoma, affecting 50 per cent. of the workers. These cases are very much like some of the roentgen-ray cancers and the cancers that sailors and other outdoor workers have. Epithelioma of the lower lip is practically never dealt with by dermatologists in our country. We send these cases to the surgeon. Everyone is agreed as to the importance of early diagnosis.

Hebra is reported to have had four cases of lupus carcinoma. I have had four in my wards at one time. In the early years of roentgen-ray treatment, we had cases of lupus from all over the country. Like everybody else, we did not know its dangers and gave doses which would be regarded as criminal now and the number of those patients who have developed carcinoma since that time is appalling. I think I have had between fifty and sixty cases of lupus carcinoma from this cause. If the patients could all be kept under observation one would not need to worry. I have operated at least twenty times in one case for the removal of carcinoma. But when one gets people of moderate intelligence, who know the dangers, and after having had one roentgen-ray cancer removed come up a few years later with a growth the size of a walnut, it makes me consider very seriously whether we ought to advise roentgen rays in the treatment of lupus. Where it has developed, the dermatologist can manage it better than the surgeon. The prognosis is bad enough, but all patients I have seen and operated on have lived some years, and some of them many years.

As to keloid, I have always been of the impression that excision is the worst possible treatment, but I have not tried excision in connection with roentgen-ray treatment. I have come to regard radium as the proper thing for these cases. Where it was not available I have had excellent results from carbon dioxid snow.

Dr. William Carpenter MacCarty, Rochester, Minn.: Many men working on epithelioma lay more stress on tobacco as an etiologic factor. My associate, Dr. Broders, recently published a very interesting study of epithelioma, in which he adheres to the probability that tobacco plays a rôle. Very little is ever said about the effect of sunburn. Having studied the skin of a few thousand farmers in the Northwest, who are exposed to the sun, and after studying epithelioma in many of them, I believe that sunburn plays an enormous part in the development of these growths, perhaps even a greater rôle than does tobacco. The lips of the farmers are always sunburned in the location in which epithelioma is most common. In my experience, epithelioma arises usually from the outer portion of the lip and not inside next the gum. Almost daily, in our clinic, patients, their relatives, nurses and physicians come in to inquire whether or not to have a mole removed, and I advise against this procedure unless the mole presents some definite change or is in a location subject to frequent injury. Speaking of epithelioma as types, Dr. Broders has shown that a single epithelioma may contain prickle cells, a glandular arrangement of the cells, and often a squamous epithelioma, frequently in the same section, so I do not believe that a basal cell epithelioma is as much of a type as we have thought. In connection with carcinoma of the stomach I found that the patients who had been operated on and had an advanced degree of differentiation of cells lived much longer than the patients with no differentiation. An epithelial pearl is the result of a high degree of differentiation.

Dr. Smith's contributions to the subject of neoplasia are, perhaps, the most valuable that have ever been made. I believe, firmly, that the secret of cancer will be found by a biologist and not by a pathologist.

Dr. John E. Lane, New Haven, Conn.: It was intimated that we might abandon surgical procedures for cancer of the lower lip in cases in which metastasis has begun, the question being asked whether radiotherapy might not be as effective as ablation. While there has been great improvement in the technic of radiotherapy recently and in the results of it in carcinoma, it seems to me that in the present state of our knowledge we must answer that question with an emphatic "No." For the present the best procedure appears to be ablation followed by radiotherapy. Radiotherapy should not be neglected in inoperable cases, as there is frequently a good chance of arresting the progress of the disease for a time and an occasional unexpected cure is made. Dr. Williams' position as to the removal of moles is sane and conservative. In case of the deeply pigmented moles, however, it would seem wise to excise them or destroy them with the cautery whenever possible. It is frequently too late to save the patient's life after such moles begin to show signs of activity. I can see no point to Dr. MacCarty's advice to patients not to have moles removed. If moles are an annoyance for any reason, even that of unsightliness, I can see no objection to removing them. It can be done without much scarring and there are practically no ill effects from their removal.

Dr. Augustus Ravogli, Cincinnati: The small growths which seem to be entirely insignificant and which last sometimes for one or two years without producing any trouble are often the beginning of an epithelioma, and do not presage anything less than the fight of the cells against the entrance of the periblastic element. When the cancer is present in the epidermis, we have epithelial cells of pathogenic nature making their way into the tissues of the derma. The normal cells put themselves on the defensive to stop the invasion of the heteroplasic cells. This forms a kind of pearl, as we term it. When the cells begin to get down into the corium and the derma, the collaginous textures try to involve these cells, and they form the alveoli, which contain some of the large epithelial cells which constitute the exact features of the cancer of the skin. It is merely an effort of the living organism to stop the progress of these cells. I have seen this epithelial infiltration go deep into the ducts of the sweat glands and invade the coil glands and from there invade the other tissues of the deep corium. The epithelioma following the roentgen-ray burn is the result of a parasitic infection. A few years ago I exhibited a case of cancer en cuirasse. The growth extended over the whole breast. It was the consequence of a burn from roentgen rays.

As to the keratoses and precancerous conditions, I do not see any difference between them, except that the cells are limited to the epidermis. When these cells have a chance to invade the corium, cancer follows. The bite of an insect or any irritation in the vegetable world is capable of causing tumor, just as in the animal tissues.

Dr. William H. Guy, Pittsburgh: The results reported, excellent though they are, should not be contrasted with statistics that surgeons furnish. The greater number of men who are doing this work have come to the conclusion that any one may obtain as good or better results with radium and roentgen rays than with surgery, regardless of whether or not neighboring metastases have occurred. Because of poor surgical results, most careful surgeons refer these cases for radiotherapy alone or combined with surgery either as a preoperative or a postoperative procedure. Some of the previous speakers have mentioned the bad results from roentgen rays, in contradistinction to those obtained with radium. In the smaller type of growth these bad results can be obviated by screening with lead up to the margin of the growth, so that the roentgen ray does not fall on any but diseased tissue. I believe that as good or better results can be obtained with radium, because a smaller dose can be applied and because we are shooting with a rifle instead of with a shotgun, and the radiation from the gamma ray will reach to the greatest possible extent the depth of the lesion. I understood Dr. Pfahler to say that he recommends excision only in the larger growths, and I agree with him. In the not too extensive case one may obtain just as good results without excision, except that a considerable amount of time may be necessary to obtain that result.

Dr. J. M. King, Nashville, Tenn.: I have seen a few cases of carcinoma of the face completely relieved by extirpation of the glands, followed by roentgen-ray treatment. I have removed some keloids and followed the excision with the roentgen rays, with very good results. I have treated some keloids on the face one inch thick with a screened Coolidge tube and have obtained excellent results. Extirpation would probably have resulted in worse scarring than from the roentgen ray alone. I had a patient who when 19 years of age was stung by a wasp on a mole just below his left eye. This soon developed into a carcinoma. When he was about 21, the growth was about the size of a quarter of a dollar. The acid from this sting might have been the etiologic factor in this case. Many more carcinomas are found in the stomach and about the cervix uteri than in any other part of the body. Perhaps some acid substance excites the production of the cancerous cell.

Dr. Richard L. Sutton, Kansas City, Mo.: About eight years ago, Dr. Lain first spoke to me about his method of clinical classification, a plan which has recently been worked out pathologically, and in a most admirable manner, by Broders. At that time, I had always been firmly of the belief that all cases of squamous cell carcinoma of the lip should go to the surgeon first, and afterward to the radiotherapist. Dr. Lain succeeded in convincing me, however, that many of these cases, especially if taken early, can be cured by radium and the roentgen ray. Hazen and Bloodgood have shown that the majority of carcinomas in this region are of the prickle or squamous cell type. Seborrheic keratoses should be divided into three distinct groups: (1) keratoses of the nevoid type, (2) keratoses of the verrucose type, and (3) keratoses of the keratoid type. The last named is the most dangerous of the three. This is the type to which Dr. Hazen ascribes the high percentage of malignancy. The point brought out by Dr. McCarty is important. In my opinion, tobacco plays an important part in the causation of these lesions. Frost bite also is a prominent predisposing factor in some instances. With regard to the treatment of keloid, Dr. Pfahler's suggestion is a good one, and I shall give it a trial. In combating the smaller lesions, carbon dioxid snow is a valuable agent, as Pusey, Norman Walker and others have shown.

Dr. Harold N. Cole, Cleveland: Tobacco has been largely responsible for carcinomas around the mouth. These growths rarely occur in women. Perhaps in the next generation we shall see more since so many women now smoke.

Dr. William C. MacCarty, Rochester, Minn.: I did not intend to say that tobacco has nothing to do with the production of epithelioma, but that I believed that sunburn was also an important factor, and that when we know the truth we may find out that it is more important than tobacco. I dare say that 75 per cent. of the people in this room use tobacco in some form, but probably none of us has an epithelioma of the lip.

Dr. Howard Morrow, San Francisco: We might divide these carcinomas of the lower lip into the deeply infiltrated and those without much infiltration. I do not think it matters whether the superficial ones are treated with radium, roentgen rays or proper excision. Superficial carcinomas should not be treated by any other methods than those mentioned. Treatment with liquid air and other caustics is still mentioned in many textbooks, but we should not adopt this form of treatment, because it is dangerous. I have had many cases of keloid treated by excision and subsequently by radium therapy and the results have been most gratifying.

Dr. George E. Pfahler, Philadelphia: I have succeeded in curing practically every one of 100 patients with epithelioma of the lip who did not have any metastases in the glands, and who had not been treated previously by caustics or surgical incision. No other treatment can equal that result. The treatment has been, as a rule, the local electrocoagulation of all areas of the disease, including about one-eighth inch around the growth, by means of the high frequency current. I then treat the lip area and the glandular area, usually with the roentgen rays. The same result can be accomplished with radium if you have enough of it, and in none of these cases have metastases developed in the glands. The diagnosis could not be questioned.

When metastases were present in the glands, I have asked the surgeon to excise them and then I treat the whole area thoroughly with deep roentgen-ray therapy. Recently I began to treat a few patients by the introduction of radium needles into these metastatic tumors. I would like to see Dr. Smith carry on the study of irritation. I believe we would learn a great deal about the histology and development of these tumors, and about the effects of radium.

Dr. Everett S. Lain, Oklahoma City: I was pleased to know that the etiologic factors as recorded from larger numbers of patients closely correspond to my own findings. Most of the lower lip cancer patients are those who are out in the open air and are subjected to sunburn. Most frequently they are thin skinned blonds. I am certain that sunlgiht is a predisposing factor in a large number of the cases as well as the use of tobacco. My technic was very uncertain in the early years. In recent years I have most frequently begun by using the beta and gamma rays for the first and perhaps second series of treatments. Later I use only the hard or gamma rays whether or not there is deep glandular involvement. A similar routine has been practiced in the use of roentgen rays. I have been giving one or more series of crossfire, deep roentgen-ray treatments in all cases of suspected glandular involvement, screening with 3 or 4 mm. of aluminum. Only five of my patients were women and two of these were smokers.

Dr. Charles M. Williams, New York: Classifying lip cancers into those that are readily cured and those that are more malignant will be a great help in selecting the proper treatment. Kangri cancer is believed to be caused by heat, although Ross is of the opinion that the soot and smoke are the important causative factors.

Dr. Earl D. Crutchfield, Galveston, Tex.: There is a distinct basal cell type of cancer which may clinically be considered a nonmalignant growth. The differentiation of prickle cell carcinoma and basal cell carcinoma is simply one of definition. I have seen two cases, both of the basal cell type, and the gland metastases were of the squamous cell type. Pearls are not more malignant, but in many of the rapidly growing types and the rapidly infiltrating types there is a tendency toward degeneration of the epithelium. On the other hand, many of these tumors show no pearl formation. I think the stage in which the cells divide has much to do with classification.

Dr. Erwin F. Smith, Washington, D. C.: All I have wished to do all these years was to get the oncologists to see things in a new light and not depend chiefly on section cutting, not that I deprecate that, but that I conceive something more and different to be necessary. If I can wake them up to that, I think I have done my share of work even if I do not make any animal experimentation. Already cancer specialists have begun to study crown gall from their own standpoint, not only in the United States, but also in England, Germany and other countries, and C. O. Jensen of Copenhagen, is on record as saying: "I fully share the opinion of Erwin F. Smith that crown gall is a new formation which (irrespective of its cause) can be placed side by side with the real malignant tumor formation in the higher animals."

THE EFFECT OF MERCURY SALICYLATE ON THE WASSERMANN REACTION

OBSERVATIONS ON THE SEROLOGY OF EIGHTY-SEVEN PREVIOUSLY UNTREATED MEN

HERMAN GOODMAN, B.S., M.D.
NEW YORK

I have recently had the opportunity of treating a number of syphilitic patients solely by the intramuscular injections of mercury salicylate. The paucity of reports of the effect of this drug alone on the Wassermann reaction is deemed sufficient reason for the publication of this study.

TREATMENT OF SOLDIERS WITH MERCURY SALICYLATE

The eighty-seven patients were men in the military service who had no active manifestations of syphilis. They had all passed the clinical examination of the draft board and that of the enlisting officers. Some of the patients were selected by the routine serologic examination of cooks and bakers, and candidates for these positions.[1] Thirteen of the patients denied having had syphilis. Twelve of these gave a 4 plus Wassermann reaction on more than one examination; the other presented a scar on the penis and scars of bilateral suppurative adenitis. One of the patients was an hereditary syphilitic.

No case in which the patient received arsphenamin previously or concomitantly with the mercury injections is reported in this paper, nor cases in which patients had received previous systemic antisyphilitic treatment as civilians. I am, therefore, unable to report the action of mercury salicylate on the Wassermann reaction in active syphilis. I did not feel justified in withholding from patients with active manifestations of syphilis the chemotherapeutic drug arsphenamin.

The serology was performed at the laboratory of the Institute of Tropical Medicine and Hygiene, San Juan, P. R. The only information the laboratory received was the infirmary number of the patient. The tests were made in duplicate. A clinical control, known positive, was always sent in, and the laboratory had no means of identifying this control. Not infrequently, and with the knowledge of the laboratory director that it was being done, two tests of the same patient, taken at the same time, were put through on the same day, one test by name and the other by number. This ruse, as it might be called, was an impetus to the clerical and technical force which assured me that few, if any, errors of disinterest would occur. In all I was able to correlate the serologic and clinical findings in over 2,500 patients, and I am assured that the tests are trustworthy and do not hesitate to base conclusions on them.

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[1] Goodman, H.: Genital Defects and Venereal Diseases Among the Porto Rican Draft Troops, J. A. M. A. **72**:907 (March 29) 1919.

METHOD OF PROCEDURE

The patients who were given the mercury salicylate treatment had the Wassermann reaction performed at the first visit. Subsequently, for six or eight weeks, they received 1 grain of mercury salicylate in liquid petrolatum. The 10 per cent. suspension was prepared by my pharmacist under the most strict aseptic precautions. The site of injection was the region of the buttock, alternating from one side to the other. Extra long needles were used, sharpened and sterilized after each injection. The Luer all-glass syringe was employed. The dose was not increased progressively. After a course, another Wassermann test was taken, and then a rest of four weeks with freedom from treatment was given. I had planned to have another Wassermann test made before resuming treatment, but few of the patients reported received this test as the demobilization intervened.

RESULTS

Forty-seven patients showed no change from 4 plus or 3 plus positive reactions after the first course of mercury salicylate. In five patients the Wassermann advanced from 3 plus to 4 plus. In seven patients the reaction was reduced from 4 plus to 3 plus. There were in all fifty-eight patients, or 66 per cent. with minor or no change from very strongly and strongly positive reactions. In one patient there was a reduction from 3 plus to 2 plus. In five cases there was recorded a diminution from 4 plus to 2 plus. In four other cases there was a change from 4 plus to doubtful.

In eight patients, or 9 per cent. of the total, there was a reversal of the Wassermann reaction from 4 plus to negative. In four others the negative Wassermann did not persist, and a 4 plus Wassermann reaction was obtained after the rest period. In one instance the Wassermann 4 plus prior to and at the end of the first course of mercury salicylate was negative at the expiration of the rest period.

The table contains data on twenty-nine cases. Those with no change in reaction have been omitted.

Mercury Salicylate and the Wassermann Reaction *

Number	Case	Infected	First Wassermann Test	Number Mercury Salicylate	Second Wassermann Test	Wassermann Test after Rest
1	467	1912	+++	6	++	
2	632	Cook	++++	9	++	
3	636	1918	++++	8	++	
4	395	1916	++++	8	++	
5	469	1916	++++	8	++	
6	910	1918	++++	8	++	
7	746	1916	++++	9	++	
8	738	1918	++++	6	±	
9	1289	Denied	++++	6	±	
10	1164	1911	++++	6	±	
11	1056	Baker	++++	9	—	
12	1009	Baker	++++	7	—	
13	1272	1916	++++	5	—	
14	77	1916	+++	8	—	
14	Continued	....	....	8	—	
15	388	1908	++++	6	—	—
16	140	1912	++++	7	—	
17	615	Cook	++++	8	—	
18	102	1918	++++	8	—	
19	263	1910	++++	8	—	
20	187	Denied	++++	6	—	++++
21	392	1913	++++	11	—	++++
22	205	1915	++++	8	—	++++
23	181	1910	++++	8	—	
23	Continued	....	....	8	++++	
24	653	1911	++++	6	±	
24	Continued	....	....	4	++++	
25	186	1918	++++	8	—	++
26	502	1913	++++	8	++	
26	Continued	....	....	4	—	
27	335	1909	++++	8	++	
27	Continued	....	....	5	±	
28	91	1909	++++	7	++++	
28	Continued	....	....	6	—	
29	250	1913	++++	8	++++	—

* My copy of the history of cooks and bakers does not contain any notes concerning date of infection.

LITERATURE ON TREATMENT OF SYPHILIS WITH MERCURY SALICYLATE

Although the literature is replete with articles on the use of mercury salicylate in the treatment of syphilis, they are for the most part from the pre-Wassermann period. Many, since the introduction of the reaction, deal with the technic of the intramuscular injection, and methods of rendering it less painful or even painless. Nelson and Anderson,[2] however, reported in 1915 on the use of mercury salicylate in syphilis. The Wassermann tests were made by Craig, and the results were 2 plus, plus, doubtful and negative. The patients in a military prison had not received any previous therapy. There were forty-three latent and seven secondary cases of syphilis. The dose of mercury salicylate was 1½ grains once a week in the beginning, then once in fourteen days, and later irregularly. No patient was salivated; they were all kept at work; few complained of sore buttocks, and there was no objection on the part of the men to the form of therapy. Of the action of mercury salicylate, these authors are of the opinion that: "In the light of our experience it seems improbable that the salicylate alone and unaided possesses any real curative value in this disease. . . . Serum reactions have in some cases varied from double plus to plus minus or minus, and later returned to the double plus while the treatment was in progress. It is our opinion that these variations in the serum reaction are due to other causes than the treatment. . . . It is certainly fair to believe that mercury salicylate used hypodermically in full doses over many weeks of time has little if any real influence on the disease."

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[2] Nelson, K., and Anderson, E. A.: The Use of Mercury Salicylate in Syphilis, with a Record of Its Influence on the Wassermann Reaction in Fifty Cases, J. A. M. A. **65**:1905 (Nov. 27) 1915.

These authors give a table of their fifty cases with the Wassermann reaction reported for each month the men were under treatment. The number of injections vary between twelve and twenty; the number of Wassermann reactions varies between six and eight. Two patients gave "two and three negative serum reactions. In both cases the men obtained clemency and were discharged from the prison at this period of treatment and we were unable to follow them further. It is our belief that a continued record on these two cases would undoubtedly have shown a positive reaction later in the treatment. Had they failed to do so they would have been the first to record this, for just this thing did occur in ten cases. This also clearly establishes the value of more than one serum reaction and the error that would arise from the acceptance of a single negative result as final."

Best[3] gave larger doses than Nelson and Anderson, and at weekly intervals. He writes, "the intramuscular injection of mercury salicylate offers the most convenient, most easily controlled, most efficient, and most satisfactory of any of the various forms of mercury treatment." The ten cases he cites do not, however, compare with those of Nelson and Anderson or those recorded in this paper, because seven of the patients had received previous arsphenamin therapy, and all had taken iodids.

Haller[4] reported a group of twenty-five patients in various stages and of various age of infection with 4 plus Wassermann reactions who were treated with mercury until the Wassermann reaction became negative. Treatment was discontinued until the reaction again became positive (4 plus). The average length of time until this occurred was about one month. The extreme case on the one hand was ten days, on the other hand four months. The more active the case, the more readily the reaction returned 4 plus, as one would naturally expect. The age of the infection seemed to make little difference in the rapidity of the return to positive. Variations from month to month in the degree of positiveness of serum of untreated syphilitic patients varied slightly.

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[3] Best: Intramuscular Injection of Mercury Salicylate in the Treatment of Syphilis, Med. Rec. **89**:473, 1916.

[4] Haller, David: Variations in the Strength of Positive Wassermann Reactions in Cases of Untreated Syphilis, J. A. M. A. **66**:882, 1916.

Fordyce, Swift, Craig and others have for many years taught that the negative Wassermann reaction during or after treatment is of no convincing value of cure unless it remains negative for at least two years, with no development of symptoms, no suggestion of positiveness in the reaction frequently repeated during the period of observation, and of course the negative and assuring clinical, neurologic, and serobiologic examination of the nervous system and the spinal fluid. With the first of these as a criterion, it appears that mercury salicylate alone and in the doses given has shown little evidence, from my own short period of observation on this series, or the longer period of observation of Nelson and Anderson, as qualifying as a curative agent in latent syphilis.

Should a similar opportunity present itself again, I shall give mercury salicylate intramuscularly in increasing doses from 2 to 2½ grains each week, if the patients give no evidence of mercurialism.

SUMMARY

Eighty-seven previously untreated latent syphilitic patients with 4 plus Wassermann reactions were given 1 grain of mercury salicylate intramuscularly at weekly intervals for courses of from six to eight injections. The Wassermann reaction immediately after treatment remained strongly positive in 66 per cent. of the cases. In only 9 per cent. was there a reversal to negative; and in some such patients who were given a third Wassermann test after an interval without treatment, the reaction was positive. It seems fair to conclude with Nelson and Anderson, who carried on a similar study in 1915, that mercury salicylate alone in the dosage and for the period given does not qualify as a curative agent in syphilis. The plans for a longer study were curtailed by the demobilization. In the future, mercury salicylate will be used in increasing doses up to 2 and 2½ grains weekly in an effort to learn whether mercury salicylate in larger doses is effective.

I acknowledge the aid given in this study by Dr. Rivera of San German, of Pharmacist Valera of Ponce, and of the Drs. Guiterez and Gonzales Martinez of San Juan, Porto Rico.

15 Central Park West.

FOLLICULITIS DECALVANS AND LICHEN SPINULOSUS

A CLINICAL COMBINATION *

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The depilating folliculitides compose a complex and little understood group of dermatoses, as is indicated by the variety of names given to these conditions by different authors. The terms folliculitis decalvans and pseudopelade, with which we are most familiar, usually call to mind processes producing baldness of the scalp alone. The literature shows, however, that a clinical picture similar to that of folliculitis decalvans may be seen on other hairy parts of the body, either in association with the disease on the scalp, or independently. Pringle,[1] Robinson[2] and others have described cases in which folliculitis decalvans of the scalp has been associated with a similar pathologic process in other parts. Among those who have described a similar picture in hairy parts other than the scalp, and without any accompanying involvement of the scalp, are Mewborn,[3] Darier,[4] and Arnozan,[5] the latter, under the title "Depilating Folliculitis of the Limbs," describing a condition which he said he would have likened to pseudopelade if it had occurred on the scalp. Lastly, we are familiar with lupoid sycocis of Milton or ulerythema sycosiforme of Unna,[6] and ulerythema ophryogenes of Taenzer and Unna,[7] two conditions which have much in common with folliculitis decalvans.

This paper is not concerned, however, with folliculitis decalvans associated with similar lesions elsewhere, but rather with the combination of folliculitis decalvans on the scalp, and lichen spinulosus on the body. Attention was first given to this combination when Graham Little[8] presented a case before the Dermatological Section of the Royal Society of Medicine in 1915, and it is interesting to note that the only other two cases on record were seen in Great Britain

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

1. Pringle: Brit. J. Dermat. **7**:117, 1895.
2. Robinson: Jour. Cutan. & Gen.-Urin. Dis. **23**:268, 1905.
3. Mewborn: Jour. Cutan. & Gen.-Urin. Dis. **22**:589, 1904.
4. Darier: Ann. de dermat. et syph. **32**:58, 1901.
5. Arnozan: Ann. de dermat. et syph. **23**:491, 1892.
6. Unna: Monatsh. f. prakt. Dermat. **9**:134, 1889.
7. Taenzer: Monatsh. f. prakt. Dermat. **9**:197, 1889.
8. Little: Brit. J. Dermat. **27**:183, 1915.

in the same year, the second one being presented before the same society by Dore,[9] while the third one was described in detail by Wallace Beatty[10] of Dublin.

REPORT OF CASES

CASE 1.—*History.*—Little's patient was a woman, 55 years of age, sent to him by Dr. Lassueur of Laussane, who wrote "The aspect of the skin seems to me to recall lichen spinulosus, especially the lesions of the flexual folds and the armpits. But the condition of the scalp is very unusual, and I am altogether embarrassed to make a diagnosis which fits in with the skin affection." The condition had begun ten years before, when the patient developed an inflammatory condition of the vertex of the scalp which resulted in a slow shedding of the hair and the development of bald patches. Subjective symptoms were lacking, and the trouble was ignored. Five months before Little saw the patient a similar, although much more rapid, inflammation accompanied by great itching, became apparent on the side and front of the scalp, and the hair came out in handfuls; at the same time an itchy eruption was manifest in the axillae, groins and the flexures of the elbows. In these positions there was a folliculitis in grouped patches with a general resemblance to lichen spinulosus, while on the back and on the exterior surfaces of the upper arms there was a diffuse, slightly spiny folliculitis, also itchy and reddened. The hair of the scalp, axillae and groin had been almost entirely destroyed, but the atrophy apparent in the scalp was not yet present in the axillae and groin. Little said that the condition on the scalp was obviously familiar under the name of folliculitis decalvans. He had thought of Darier's disease, but the distinct alopecia and the exclusive follicular location of the lesions in the case excluded that diagnosis.

Discussion of Case.—In the discussion which followed the case presentation. all of the speakers — Pringle, Morris, Adamson, Sequeira and MacLeod — agreed that the condition on the scalp was folliculitis decalvans, but there was a considerable difference of opinion as to the nature of the eruption on the body, some of the speakers considering it a possible early form of Darier's disease, while others were convinced that it was not. In a later discussion, however, Little asserted definitely that it was a true lichen spinulosus.

CASE 2.—*History.*—Dore's[9] patient was also a woman, aged 43. The case bore a rather close resemblance to that of Little's. A typical folliculitus decalvans had been present for two years. Nine weeks before she was shown she developed a follicular eruption indistinguishable from lichen spinulosus on the abdomen, back, chest, thighs, neck and ears. This eruption consisted chiefly of minute, scattered, skin-colored, acuminate or spiny noninflammatory papules; a few were larger, and reddened or excoriated.

Discussion of Case.—In discussing this case, Little stated that the body lesions in his case were more definitely spiny than those in Dore's, and that he considered the spiny eruption in Dore's case a coincident lichen scrofulosorum, while Adamson felt that all that could be said about the condition on the body was that it was a folliculitis.

CASE 3.—*History.*—Beatty's[10] case was carefully investigated and reported in detail. The patient, a woman of 43 years, had an eruption on the scalp and upper part of the body, presenting a combination of cutaneous symptoms unlike any combination which he had seen previously. He said only the scalp suggested folliculitis decalvans; the condition on the body resembled lichen spinulosus as occasionally seen in children, though of a coarser kind. The hair had begun to fall ten years previously, coming out in patches, gradually, without soreness, until after some years an almost universal baldness was produced. Itching of the head was at times troublesome. The eruption on the body began a month before Beatty saw the patient, appearing as a "roughness of the skin." The upper part of the chest anteriorly was first affected, but the condition spread and similar roughness appeared on the scalp.

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[9] Dore: Brit. J. Dermat. **27**:295, 1915.

[10] Beatty: Brit. J. Dermat. **27**:331, 1915.

Examination.—This revealed a scalp of cicatricial aspect, smooth and bald, throughout the greater part. Here and there were small, hard islets of follicular prominences, and formed by an accumulation of dry, horny material, some of them were pierced by short hairs. These groups of follicular plugs developed in association with the eruption on the body. On the neck, body and limbs were groups of follicular elevations, some with prominent horny spines such as are seen in lichen spinulosus of children. This eruption was widespread, but there were few lesions on the lower portion of the trunk. They were all follicular, there was a universal tendency to grouping, and the color varied from flesh color to reddish brown. The spines in the smaller lesions were fine and hairlike, and blunt in the larger lesions. They could be picked out intact, leaving a gaping folliculiar opening.

In his remarks, Beatty states that he was struck by the resemblance of his case to that of Graham Little's, a history of shedding of the hair dating back some years, followed by an acute condition like lichen spinulosus on the body. Little's and Dore's cases and his own had led him to believe that the combination of these two conditions, which he had at first regarded as merely accidental, constituted a clinical unity. He proposed calling this combination of atrophic baldness of the scalp and lichen spinulosus "Lassueur's and Graham Little's syndrome." Tissue examination in this case showed the "corps rond" described in Darier's disease, the "psorosperms" being few and discovered only after the study of a large number of sections. As Webber says, if these bodies are to be considered pathognomonic of this disease, then his case must be regarded as an atypical Darier's disease.

Case 4.—*History.*—My patient was a woman, aged 30, seen in Dr. W. A. Pusey's practice, in October, 1919. The disease began when she was 9 years of age. At that time her hair began to fall rather rapidly, the alopecia being permanent. This alopecia has been slowly progressive since that time. Eight years ago she developed an eruption over the back which she says was similar to the present attack, but it cleared up spontaneously. The present exacerbation began four or five months before the patient was seen. The first lesions appeared over the nape of the neck, followed by others over the occipital region, shoulders and back. This condition was complicated in September, when a number of boils appeared over the scalp and back. The hair had been shed rapidly again after this eruption appeared on the body. The patient's personal history disclosed nothing of interest. Her general health had always been good, and she had never had any serious illness. She suffered from chronic constipation, but had used laxatives regularly and had a daily bowel movement. Menstruation was regular and normal. The Wassermann reaction was negative.

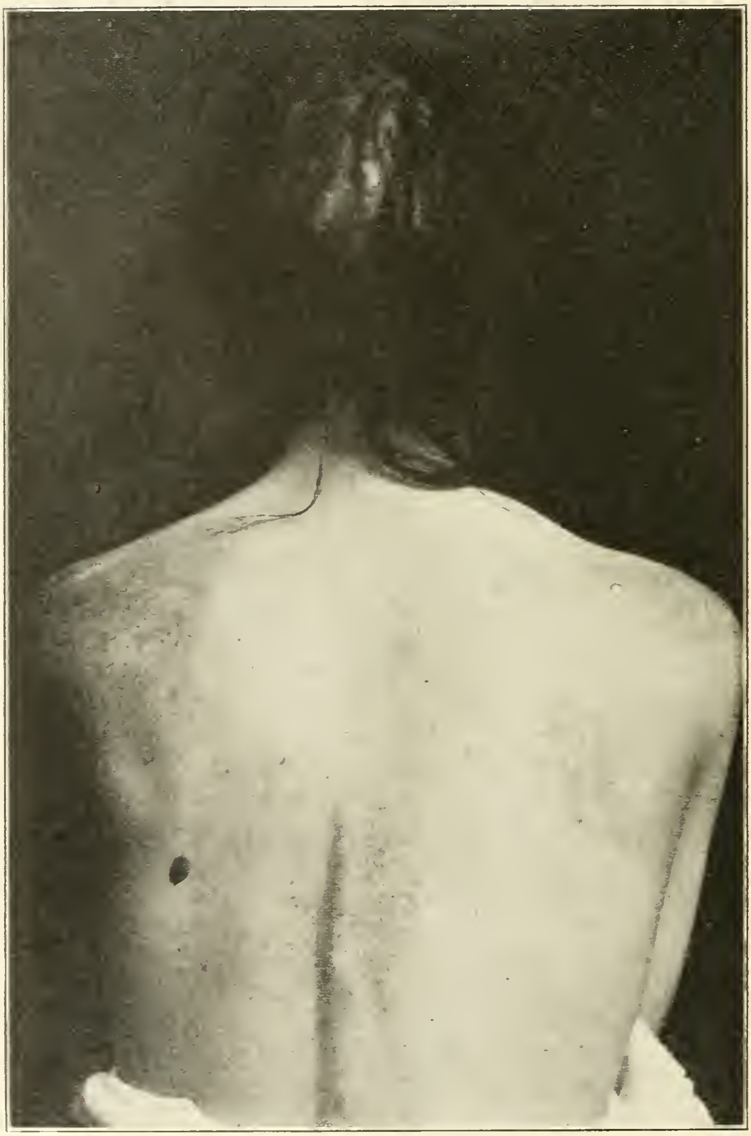
Examination.—This disclosed two clinical pictures. The scalp showed an extensive alopecia, most of the hair having disappeared, while the remaining hair was found in patches, as shown in the photograph. The skin of the bald areas showed an extreme atrophic scarring of the type seen in folliculitis decalvans. The process which had produced this atrophy was still active, numerous follicular papules and a few pustules being present. The other eruption, involving the nape of the neck, lower occipital region, shoulders, back and upper arms, consisted of variously sized groups of follicular lesions. The individual lesions varied from reddish follicular papules, slightly elevated, to definitely elevated and spinous lesions, some of them having rather long, slender spines. In the largest patches the lesions had slightly inflammatory areolae, so that the group picture showed an erythematous background with elevated follicular lesions. In the smaller groups the erythematous background was lacking, showing it to be secondary. Removal of one of the spinous lesions left a dilated follicular orifice. The lesions varied from a grayish to a reddish color, while the group was dull red. The patient, who was refractory, refused biopsy, and passed from observation before any therapeutic attempts could be made.

SUMMARY AND COMMENT

All of these four cases occurred in women, aged, respectively, 55, 43, 43 and 30 years. In all, folliculitis decalvans was of long standing (ten, two, ten and twenty-one years, respectively), followed by the rather sudden development of a follicular eruption of the body whose clinical picture was that of lichen spinulosus. In all cases the condition on the scalp was obviously folliculitis decalvans, but the body eruption was more puzzling. In the discussion of Little's case, an early Darier's disease was considered, but Little had been able to rule this out to his own satisfaction, and in a later discussion stated definitely that the condition was lichen spinulosus. Dore considered the eruption in his case to be clinically indistinguishable from lichen spinulosus, as did Beatty in his case, although it will be recalled that the histologic picture suggestive of Darier's disease was disturbing. In my case no suspicion of Darier's disease could be entertained. The exclusive follicular location of the papules, the distribution of the eruption, the extreme alopecia, the lack of a greasy seborrheic element, the grouping and the spinous character of the lesions readily eliminate that disease. I am convinced that this combination is not to be regarded as merely an unusual keratosis follicularis.

No attempt has been made to explain the association of these two conditions, and this is not surprising when we consider that we are dealing with two conditions, each of obscure etiology. Coincidence would scarcely serve as an explanation, since each of them is an uncommon disorder. It is difficult to consider the eruption on the body as folliculitis decalvans, since in none of the four cases was there any atrophic scarring in the body lesions, as is the case when folliculitis decalvans affects parts other than the scalp. Furthermore, the body eruption was too acute.

I wish to suggest, however, one hypothesis which is founded on a comparative basis. We are familiar with other follicular eruptions, which are looked on as manifestations of the activity of toxins secreted



Alopecia and eruption over back, neck and shoulders in Case 4.

by infectious organisms affecting distant parts of the body. The most familiar example of this kind is the lichen scrofulosorum type of tuberculid. More recently we have become acquainted with the group of trichophytids, first described by Jadassohn in 1911, consisting for the most part of lichenoid eruptions occurring on the body of children affected with trichophytosis capitis, usually kerion celsi. In a number of these cases the eruption assumed a type clinically indistinguishable from lichen spinulosus, as shown by Jadassohn,[11] Bloch,[12] Guth,[13] Rasch [14] and others.

In the condition under consideration we have some points in common with the above conception of the etiology of lichen scrofulosorum and lichenoid trichophytids; folliculitis decalvans being almost certainly due to a chronic infective process, which, theoretically at least, might be able to elaborate toxins responsible for the production of lichen spinulosus. In support of this view may be offered the opinion of Adamson,[15] who is probably best acquainted with lichen spinulosus; he suggests that a toxic etiology is the most plausible one for the condition. Furthermore, in at least two of the cases (Beatty's and my own), the process on the scalp, as evidenced by the alopecia, had become more active at the time of appearance of the lichen scrofulosorum; and we know that in the case of the tuberculids, the eruption often appears at a time when the tuberculous process has been lighted up by some factor, as in the case of lichen scrofulosorum following measles. The above hypothesis is offered, it should be understood, only as a suggestion, for I had no opportunity to study the patient with this view in mind.

In conclusion, I should like to say that this paper was offered to call attention to this combination of clinical conditions in the hope that recognition and study of other cases might result in a better understanding of its significance.

ABSTRACT OF DISCUSSION

Dr. J. M. King, Nashville, Tenn.: I had a patient who had lichen spinulosus, but I do not recall that she had any disturbance of the hair or folliculitis. The hair growth was poor and thin; she complained of itching but had no scalp involvement. The diagnosis in this case was confirmed by Dr. George MacKee and Dr. Howard King.

Dr. F. W. Cregor, Indianapolis: We do not have as much folliculitis decalvans in this country as in Europe. I recall seeing many boys in the clinics there begging to be relieved of the scars following this disease that they might emigrate to America. I have not observed lichen spinulosus in any cases of folliculitis decalvans. I have observed, however, lichen spinulosus following lichen ruber planus in two patients, both of whom had received arsenic for more than 120 days. I think that arsenical medication had something to do with the process in Dr. Senear's case.

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[11] Jadassohn: Autoreferat i, Cor.-Bl. f. schweiz. Aerzte, **42**:24, 1912.

[12] Blocki: Die Allgemein-pathologische Bedeutung der Dermatomykosen, Halle, p. 82, 1913.

[13] Guth: Arch. f. Dermat. u. Syph. **118**:856, 1914.

[14] Rasch: Brit. J. Dermat. **28**:9, 1916.

[15] Adamson: Brit. J. Dermat. **17**:39, 1905.

Dr. Walter J. Highman, New York: I had a patient with what I thought was pityriasis rubra pilaris on the body and patches on the head of what seemed to be alopecia areata but which proved to be pityriasis rubra pilaris.

Dr. Oliver S. Ormsby, Chicago: In November, 1919, I presented a patient before the Chicago Dermatological Society with a condition which was practically identical with that reported by Dr. Senear. It was presented as an example of folliculitis decalvans and lichen spinulosus. I think five cases are now on record. The patients all had a similar history and probably represent a disease group which has not heretofore been reported.

Dr. Francis E. Senear, Chicago: Dr. Ormsby's case and mine corresponded in nearly every detail in the clinical picture, except that the scalp involvement in my case was more extensive than in Dr. Ormsby's case. Arsenic might well furnish a basis for the development of lichen spinulosus. In the English literature there is not infrequent reference to the development of spinous lesions in lichen planus, similar in character to those of lichen spinulosus. It is possible that Dr. Cregor has seen that type of lichen planus, but it does not seem probable that the treatment he mentioned would have cleared up the cases so readily and permanently had they been true lichen planus lesions.

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THE ASSOCIATION OF HERPES ZOSTER AND VARICELLA *

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The possibilities of this subject are obviously extensive, but space limitations will not permit more than an occasional reference to the etiology, epidemiology and immunology of zoster and varicella. I shall attempt to do two things: first, to report a case of associated herpes zoster and varicella which in some of its relations is almost unique in medical literature; and second, to present certain recommendations deduced from an examination of the literature on this particular association which, if followed, would contribute to the clarification of a subject upon which there is now great confusion.

The report presented covers a case which falls into Group 3 in the classification given below: A man with zoster developed varicella which he passed on to a daughter not otherwise exposed.

REPORT OF A CASE

History.—The patient, a physician on the house-staff of a sanatorium, in early middle life, of regular habits, in good general health and with a negative medical history, presented two sets of skin lesions involving the face, the trunk, arms and legs, and the mucous membrane of the tongue. Those on the left side of the face appeared first, being preceded for about twenty-four hours by a burning pain in the left temple of such nature and severity as to suggest the possibility of an accidental contact of the part with an acid. The lesions consisted of numerous groups of vesicles, situated on a more or less diffusely reddened integument, and containing serous material; at several places the contents were hemorrhagic. By the third day the local pain was marked; there was considerable general malaise with moderate temperature; the anterior auricular and the upper anterior cervical glands became enlarged and painful; the vesicles increased in number, some appearing on the tongue; an edema of the lids closed the left eye. The condition was obviously a rather severe zoster involving the upper and middle branch of the fifth cranial nerve. Five days after the inception of the attack, at the time when the zoster was at its height, there appeared on the other parts of the face and scalp, and on the trunk, arms and legs, lesions quite evenly distributed, forty to fifty in number, consisting of macules, slightly pruritic but not painful and quite intensely erythematous, from the center of which vesicles emerged, becoming pustular in about twenty-four hours. Some of these were umbilicated, but hemorrhagic lesions were not present. The second eruption was recognized as varicella, and the patient was placed in the usual quarantine. The zoster lesions cleared up in about twelve days, leaving a few depressed scars; the varicella disappeared after about the same length of time, leaving no trace.

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

Ten days after the beginning of the varicella lesions, the patient's 3-year-old daughter, who had been in contact with him before and during the quarantine, became ill with typical varicella. In the father's case there was no known exposure to chickenpox, and no knowledge of his ever having had that disease. The daughter had been exposed to the condition only through the father. As to focal infection as a cause of the zoster, there were no obvious foci to be found, but an exhaustive examination of the teeth and tonsils to determine the presence of infective material was not made.

CASES REPORTED IN LITERATURE DIVIDED INTO FOUR GROUPS

The number of cases of associated herpes zoster and varicella reported in the literature was placed by LeFeuvre[1] in January, 1915, at forty. Four years later, Low[2] states that over fifty have been recorded. I have been able to find somewhat less than fifty, and as a number of references were not available, the correct number is probably in the neighborhood of sixty.

For the purposes of brief review, these cases may be grouped into four classes:

1. Herpes zoster in one patient followed by varicella in others who were exposed.

2. Herpes zoster in one patient followed by varicella in the same patient not followed by varicella in others who were exposed.

3. Herpes zoster in one patient followed by varicella in the same patient followed by varicella in others who were exposed.

4. Varicella in one patient followed by herpes zoster in others who were exposed.

Group 1.—Fully two-thirds (about forty) of all reported zoster-varicella cases belong to Group 1.[3] If frequency of occurrence of cases in this group may be estimated from the number of reports of cases suddenly made in England in 1913, when in the period from May to December sixteen cases were recorded in the literature, it seems probable that since 1888, when Bokay first called attention to the association of the two conditions, a large number of Group 1 cases have occurred that have not been reported.

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[1] LeFeuvre: Brit. M. J. **1**:15 (Jan. 2) 1915.

[2] Low: Brit. M. J. **1**:91 (Jan. 25) 1919.

[3] Walker: Brit. M. J. **1**:1192 (May 31) 1913. Bruce: ibid. **1**:1194 (May 24) 1913, and **2**:584 (Aug. 30) 1913. Cressy: ibid. **2**:528 (Aug. 23) 1913. Roberts: ibid. **2**:584 (Aug. 30) 1913. Harrison: ibid. **2**:712 (Sept. 13) 1913. Oakes: ibid. **2**:712 (Sept. 13) 1913. Coates: ibid. **2**:712 (Sept. 13) 1913. Willson: ibid. **2**:712 (Sept. 13) 1913. Milne: ibid. **2**:896 (Oct. 4) 1913. Orr: ibid. **2**:1048 (Oct. 18) 1913. Busfeld: ibid. **2**:1124 (Oct. 25) 1913. Bartlett: ibid. **2**:1340 (Nov. 15) 1913. Quinn: ibid. **2**:574 (Nov. 23) 1918. Hepworth: ibid. **2**:529 (Oct. 10) 1914. Destinn: ibid. **1**:633 (April 10) 1915. Low: ibid. **1**: (Jan. 25) 1919. Heim: Berl. klin. Wchnschr. **49**:2349 (Dec. 2) 1912. Richardson: Lancet **2**:1732 (Dec. 13) 1913. Fordyce: Edinburgh M. J. **23**:34 (July) 1919. Bokay: Wiener klin. Wchnschr. **22**:1323, 1909.

An average case of this group develops thus: The patient has an attack of zoster; in about fourteen days varicella is found in some one exposed to the zoster patient without discoverable exposure to varicella elsewhere. While these reported cases are free from serious doubt as to the correctness of the zoster and varicella diagnoses, it must be admitted that for the determination of less obvious things many are incomplete in clinical description. Such significant items as the age of the zoster patient and the location and severity of the zoster attack are not infrequently omitted. The time interval preceding the appearance of the varicella is practically always given as this seems to be accepted as an important factor in the diagnosis. In forty-eight cases of varicella originating from thirty-two cases of zoster the average interval was fourteen and one-sixth days, the extremes being two and twenty-one days. In a large number of cases the diagnosis "varicella" or "chickenpox" is given directly without description of the number and nature of the component lesions. The question of exposure of the varicella victim to other possible sources of infection is almost always considered, but in few cases is a previous varicella in the zoster patient discussed.

In explanation of these cases Bokay,[3] who himself reported nine instances of the association, advances the theory that under certain unknown conditions the infective agent of varicella produces a local zosteriform eruption instead of a generalized exanthem; the zoster is thus an expression of varicella, and contagion is readily passed to others. He quotes Henoch,[4] Thomas,[5] Jennings[6] and Swoboda,[7] in support of the theory, and proposes the term "zoster varicellosa" to designate the condition. Other advocates of the theory are LeFeuvre,[8] who suggests a clinical term of similar import to Bokay's, namely, "varicella herpetica"; and Heim,[3] in whose report the varicella lesions (in a boy: source, zoster in mother) were zoniform in the right axilla, this area being also the seat of zoster-like pain.

Group 2.—This group, in which zoster in one patient is followed by varicella in the same patient, but not by varicella in others exposed, is particularly interesting in that it brings into consideration the entire subject of so-called generalized herpes zoster. In fact, it is impossible to discuss this group without including the latter condition. Under various captions such as "Herpes and Varicella," "Herpes Zoster with Aberrant Vesicles," "Herpes Zoster and Chickenpox," "Association of Zoster and Chickenpox," and "Varicella Accompanying Herpes Zoster," a scant dozen cases assignable to this group have been reported by Orr,[3] Williams,[9] Ffrench,[10] Frances and Goldberg,[11] Downes,[12] Corlett [13] and Head.[14] Some of these reports are also lacking in clinical detail, and the diagnosis of varicella does not always seem to be free from some element of doubt. In Orr's case the varicella appeared three days after the onset of the zoster and was "typical in character and distribution." In Williams' case the zoster lesions merely "looked like chickenpox," and as there appears to have been no general distribution, the case should be excluded from Group 2. In the case reported by Ffrench the interval was one day, and the only description of the generalized eruption given was the word "crop"; the diagnosis of "chickenpox complicated by herpes zoster" was made by a health officer, but Ffrench, himself, considered it a case of zoster with aberrant vesicles. In two of the cases reported by Frances and Goldberg the second eruption was "varicelliform," appearing two and three days after the onset of the zoster; in the third a varicella is described, but a time interval is not mentioned. In Downes' case the rash which appeared seven days after the beginning of the zoster was "indistinguishable from varicella," but it should be added that the patient had taken phenacetin and morphin for the zoster pain, and that several in the family who had not had chickenpox, including a new-born babe, escaped that condition, though no attempt was made at isolation. In Corlett's reported cases, the first showed lesions "strikingly like varicella in appearance and distribution" with a five-day interval preceding; the diagnosis of varicella was concurred in by an eminent colleague; the second, with a six days' interval, showed a vesicular eruption which was simply diagnosed "varicella." The notes on the third case are scant, but the eruption corresponded to those of Cases 1 and 2; the fourth, after an interval of several days, showed an eruption which conformed to that of varicella. Three of these cases were in adults past middle life. Corlett apparently did not associate the two conditions etiologically, and while recognizing the rarity of the coincidence, was apparently more impressed with the unusualness of varicella occurring in adults,

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[4] Henoch: Vorlesungen über Kinderkrankheiten, Ed. 6. Berlin, 1892.

[5] Thomas: In Ziemann's Handbuch der spec. Pathologie und Therapie, Vol. 2.

[6] Jennings: In Keatings Encyclopedia of Diseases of Children **1**:761.

[7] Swoboda: In Pfaundler-Schlozmann: Handbuch der Kinderkrankheiten, **1**:732.

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8. LeFeuvre: In Guy's Hosp. Gaz. **32**:101, 1918.
9. Williams: Brit. M. J. **2**:584 (Aug. 30) 1913.
10. Ffrench: Brit. M. J. **1**:388 (Feb. 11) 1899.
11. Frances and Goldberg: J. A. M. A. **70**:1061 (Apr. 13) 1918.
12. Downes: Brit. M. J. **1**:307, 1919.
13. Corlett: J. Cutan. Dis. **23**:289 (July) 1905.
14. Head: Allbutt's System of Medicine, Ed. 1, **8**:630.

for he adds, without giving detailed reports, that he had seen two cases suggestive of the combination in children. (This attitude of mind toward varicella in adults was found several times in the literature usually also exerting an influence on diagnosis.) Head's patient, after a one-day interval, showed "typical chickenpox spots."

In this group of eleven cases the time interval between the two eruptions in eight instances was from one to seven days, the average being three and one-half days. It should be noted that this is much less than the average time interval given for Group 1, which was fourteen and one-sixth days. In ten, the description of the second eruption corresponds to that of varicella; in one, only the word "crop" is used; in ten, the distribution includes enough of the body surface to warrant the designation "generalized." Although the second rash was in all instances diagnosed as varicella, it is extremely significant that no case of chickenpox is recorded as having developed from exposure to combined zoster and varicella. This is so contrary to what would be expected that one may with propriety question whether in every instance the diagnosis of varicella was correct. If not varicella, these cases would fall into the category of so-called generalized herpes zoster.

This term, generalized herpes zoster, is used rather loosely in the literature. It is impossible to say exactly how many cases have been recorded. Not including the reports of bilateral zoster,[15] and without considering the literature of the etiology of zoster, I have been able to find at least twenty-six cases;[16] the number is much larger if cases mentioned but not reported in detail are included. In these reports three descriptive terms are used, namely: herpes zoster with aberrant vesicles, generalized herpes zoster and universal herpes zoster. The first two terms are employed rather indiscriminately, but the last is fairly self-explanatory. A better and more inclusive designation as a substitute for this term would be "multiple herpes zoster," meaning the disturbance of more than one group — possibly all groups — of posterior root ganglions producing multiple areas of massed zoster lesions. This would include the rare instances of bilateral zoster and the oft-quoted case of universal zoster by Columbini pictured in Mracek's Handbuch.[17] But the expressions "aberrant vesicles" and "generalized" zoster need to be more clearly defined. Tenneson,[16] who originated the term "aberrant vesicles," says that they are few, isolated, look like those of the zoster group, are distributed irregularly at great distances from each other over the entire body, developing slowly, disappearing perhaps without being noticed, and occurring in nine out of ten cases. Crocker and Mracek confirm this stated frequency of occurrence. Molinié [16] says that extensive zoster always, and moderate zoster usually, shows these vesicles, and that they do not become necrotic. Unfortunately, cases fitting Tenneson's description have repeatedly been termed "generalized herpes zoster." It is, therefore, impossible at the present time to state exactly what is meant by the two terms. Fasal [16] suggests that the term "aberrant vesicles" be limited to lesions in the neighborhood of the zoster area, and that the term "herpes zoster with generalized eruption" be applied to the more extensive and intensive outbursts, thus avoiding the implication that the second rash is necessarily a zoster.

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[15] For an excellent bibliography of bilateral herpes zoster, see Stelwagon's Diseases of the Skin, Ed. 7, Philadelphia, W. B. Saunders Company.

[16] Pernet: Brit. J. Dermat. **26**:399, 1914. Schamberg, J. F.: Generalized Herpes, J. A. M. A. **54**:532 (Feb. 12) 1910. Arkwright: Quoted in London Lancet **2**:1223, 1900. Fasal: Arch. f. Derm. u. Syph. **95**:27, 1909. Haslund: Nordisk. Med. Archiv., Vol. 8, 1897; and Kaposi's Festschrift, 1900. Weidenfeld: Arch. f. Derm. u. Syph. **96**:87, 1909. Uhlmann: ibid. Ehrmann: ibid. Lipschultz: ibid., quoted in Steuer's article (see below). Mackay: Glasgow M. J. **48**:278, 1897. Janselme and Leredde: In Lancet **2**:822, 1898. Tenneson: Traité de Dermatologie, Paris, 1893. Girandeau: Bull. de la Soc. d. hôp., Seance du July 29, 1898, quoted by Fasal. Steuer: Wiener klin. Wchnschr. **61**:1167, 1911. Molinié: These de Paris, No. 97, 1895-96. Beyer: Arch. f. Derm. u. Syph. **78**:233, 1913. Tryb: Dermatologische Wchnschr. **59**:983, 1914. Fischl: Arch. f. Derm. u. Syph. **118**:553, 1913. Nobl: Wiener klin. Wchnschr. **24**:14, 1911. Parkes Weber: Internat. Clin., Ser. 26, **3**:185, 1916.

It is obvious that the "aberrant vesicles" and "generalized zoster" types may closely simulate varicella, and it is especially interesting that the rash in the generalized cases is practically always described in terms which link it with the idea of varicella. Some of these expressions are: "suspected of being smallpox but looked like chickenpox;" "like varicella;" "varicella-like spots;" "varicelliform." This similarity to varicella is apparent when the clinical details are examined more fully. Vesicles were present in fourteen cases; vesicles with opaque contents were observed in seven; with hemorrhagic contents in four; umbilicated, two; in the mouth, two; like those of chickenpox, four, and grouped, three. Papules were also present in seven. Lesions appeared in successive crops in seven; areola was present in five. The number of lesions ranged from thirty to several hundred distributed practically over all parts of the body. As to time interval, in five there was none; in two, one day; in three, from four to seven days; in four no mention of time was made; the average time interval was one and seven-tenths days. Thus it is seen that this group of "generalized" zoster is strikingly like Group 2 of our classification in which varicella was the diagnosis given for the second eruption. A significant difference is found in the time interval between eruptions: namely, one and seven-tenths and three and five tenths days. Otherwise the similarity is so great that one questions whether the difference is not in some instances one of terms only. A varicella erroneously called a "generalized zoster" remains a varicella and vice versa.

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[17] Mracek's Handbuch der Hautkrankheiten **1**:692.

Group 3.—This group of our zoster-varicella classifications combines the clinical element of Groups 1 and 2; that is, the patient with zoster not only develops varicella himself, but passes it on to others. As mentioned above, about fifty cases in the first two groups have been reported; instances, however, which fit the requirements of Group 3 seem to be of extreme rarity. The case herewith reported is one; the generalized eruption which showed itself five days after the appearance of the zoster in a man who had never had varicella, was clinically in every detail a typical varicella, and the child who, following exposure to this zoster patient, developed varicella after a ten day's incubation period, was known positively not to have been exposed to that disease elsewhere. In the literature, up to the present, I have been able to find only two cases which might by liberal interpretation be placed in this group; neither of them is a clear-cut case. In one case reported by Grey,[18] two varicellas developed after exposure to a case of right thoracic zoster, with one or two lesions on the left chest; the diagnosis of chickenpox was made after recovery and was based on the fact that these spots outside the zoster area left "scars like those of varicella." The second case is reported by Weber:[16] A man with leukemia under treatment with arsenic developed a typical zoster about the right shoulder, five days later a generalized but scanty eruption of varicella-like lesions appeared over the body; a boy exposed to this patient left the hospital and in ten days became ill with varicella. Weber says: "It is worth mentioning, but it is doubtless a mere coincidence."

Group 4.—This group is a logical outgrowth of the preceding groups: If zoster can lead to varicella, why should not varicella lead to zoster? Four cases have been found recorded by Dando,[19] Aikman,[20] and an anomynous observer.[21] Dando reports attending a man with zoster whose son had had chickenpox four weeks before; some years before in the same family he had cared for the mother who had had a zoster which appeared five weeks after a varicella in a daughter. In Aikman's report a boy returned to a boarding school with an unhealed varicella; seven days later his teacher, who had never had varicella developed a right thoracic zoster; varicella appeared also in other

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18. Grey: Brit. M. J. **1**:377 (Mar. 29) 1919.

19. Dando: Brit. M. J. **2**:1340 (Nov. 15) 1913.

20. Aikman: Quoted by Parkes Weber; from LeFeuvre: M. J. of South Africa **9**:77, 1914.

21. Guy's Hospital Gazette **27**:219, 1913.

children. The anonymous observer reports that a boy of 13 showed a zoster two and one-half weeks after exposure to chickenpox. These cases are lacking in clinical detail and prove little or nothing; they are, however, extremely suggestive of important possibilities.

COMMENTS

From the foregoing consideration of the literature it is evident that, while an etiologic relationship in certain cases of herpes zoster and varicella must be accepted, much needs to be done toward the clarification of confused points. There is an urgent call for more careful and more complete clinical observation. Some of the items which should receive closer attention from clinicians are:

Since every patient with zoster has varicella as a possible causative factor and vice versa, inquiry should always be made of a zoster patient regarding possible exposure to and a previous attack of varicella; and every varicella patient should be questioned as to possible exposure to a zoster victim and as to previous zoster attacks.

To check up on the theory of Bokay, Heim and others, every varicella case should be examined with special reference to a possible grouped or zonaform distribution of lesions and to a history of neuralgic pain in such lesions. Incidentally, adult years must not be given undue weight in excluding a varicella.

In order to establish the correctness of the statements of Tenneson, Crocker and others as to the frequency of the so-called "aberrant vesicles," every zoster patient should be examined daily, if possible, for the presence of lesions outside the zoster area. If aberrant vesicles are found or if more extensively distributed lesions appear, in order to determine the nature of the second eruption and to establish a sound basis for differential diagnosis, a complete observation should be made concerning time relationship of the two eruptions; possible influence of drugs used in treatment; the condition of the zoster lesions when the general lesions appeared; number of the latter and positional relation to the zoster area; type or types of lesions in the general eruption; the symptom of pain; appearance in crops and observation as to whether the lesions are hemorrhagic, umbilicated, necrotic or surrounded by an areola. Every detail that might be of value in differentiating the zoster vesicle from the varicella vesicle should be searched for and noted.

Finally, as an essential step in clearing away the haze which envelops the present conception of "generalized herpes zoster," that term should be abandoned as indefinite and inaccurate and a new nomenclature established. This group should be rearranged under the captions given above, namely: (*a*) Herpes zoster with aberrant vesicles, restricting the lesions to the neighborhood of the zoster area as suggested by Fasal instead of the wider distribution of the original definition; (*b*) herpes zoster attended with a general eruption, and (*c*) multiple herpes zoster, to include bilateral and universal cases.[22]

ABSTRACT OF DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: About ten years ago I saw a patient who presented a typical and marked case of herpes zoster of the face and scalp, and on the fourth day of the zoster a generalized varicella-like eruption developed. I have never satisfied myself as to what this might be, but it belongs in one of the groups described by Dr. McEwen.

DR. EVERETT S. LAIN, Oklahoma City: A group of diseases of which herpes zoster is one, no doubt has its etiology based on some toxic product of bacterial nature. It can now be easily understood from the reports that have been made, why varicella, variola and other diseases may possibly have herpes zoster associated with them.

DR. GEORGE P. LINGENFELTER, Denver: A few months ago I saw a case of undoubted herpes zoster associated with marked neuralgic pain. This patient had been exposed to smallpox some days before. Five days later he developed typical smallpox.

DR. J. M. KING, Nashville, Tenn.: In pneumonia, concurrent with the infection, herpes simplex develops in 33 per cent. of cases, due, no doubt, to the pneumococcus. Why could there not be an organism in varicella which has a predilection for nerve tissue, thus producing herpes zoster? Both varicella and herpes zoster produce immunity. Why could not the organism of varicella produce herpes zoster just as the pneumococcus produces herpes simplex?

DR. WALTER J. HIGHMAN, New York: Herpes is a disease *sui generis* and has no connection with herpes zoster. The pathology is similar. True herpes zoster has no connection with any other disease. The zoster may be due to the same micro-organism that causes the varicella; in other words, they may be different clinical expressions of the same agency, but the zoster-like eruptions are not true zoster. The latter never recurs.

DR. RICHARD L. SUTTON, Kansas City, Mo.: I thought herpes zoster was usually due to infection or to injury of one of the posterior ganglions. I did not know that it was a disease *sui generis*.

DR. ERNEST L. MCEWEN, Chicago: I made no attempt to discuss etiology for I found the subject so broad that I could not do so in the time allowed. I am convinced that herpes zoster may have a number of infective causes.

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[22] The following references were not available:

LeFeuvre: M. J. of South Africa **12**:77, 1914; ibid. **13**:133, 1918.
Minet and LeClerque: Clinique **6**:100, 1911.
Janselme and Touraine: Bull. de la Soc. francais, de Derm. et syph. **25**:351 (July 2) 1914.
Janselme and Leredde: Bull. et mém. Soc. méd. de hôp. de Paris. **15**:619, 1898.
Watson: Guy's Hosp. Gaz. **29**:186 (Apr. 24) 1915.
Wainwright: ibid. **27**, May 10, 1913.
Heatherby: ibid. **28,** April 25, 1914.

It is possible that the organism of varicella and also of smallpox is capable, under certain conditions, of producing the clinical picture of zoster. The real purpose of this paper was to emphasize the following: first, that these cases are occurring much more frequently than the literature indicates; second, that the reports in the literature are incomplete and insufficient; third, that it is imperative that clinicians and pathologists should examine most thoroughly these cases of zoster combined with other eruptions in order to find out everything possible about them; fourth, the desirability of abandoning the term "generalized herpes zoster," and substituting for it the three terms given, as covering more accurately all the types observed. It is only by more careful and complete observation that we will arrive at a more accurate knowledge of the association of herpes zoster and varicella.

A FEW EARLY NOTES ON SYPHILIS IN THE ENGLISH COLONIES OF NORTH AMERICA

JOHN E. LANE, M.D.

NEW HAVEN, CONN.

"It is only from the most scanty materials that we can trace the origin and progressive improvements in the healing art among the early settlers of the American colonies," and American medical literature was an almost unknown product before the beginning of the Revolution. In the earliest days there were few physicians in the Colonies, and in New England "the practice of medicine was in many instances united with the parochial duties of ministers of religion, who by their amiable manners, zealous attention and pious converse, endeared themselves to their people." [1]

The population was too small to attract many physicians, and skilful men of the profession "were of rare occurrence in the colony. They seldom, it would appear, partook of the religious zeal that brought other emigrants across the Atlantic. Dr. Robert Child was one of the earliest physicians to come to New England, though he never practiced medicine there. For a long time he has been given the reputation of being "an advocate of general religious toleration and freedom of conscience," but Kittredge has recently shown that "he abhorred these principles with all the strength of his earnest soul as the devil's latest device for the ruin of society and the damnation of mankind." Instead of toleration and freedom, he, an ardent Presbyterian, was "eager to extend to all his countrymen the blessings of a rigid conformity, . . . and to subvert the Massachusetts government, to bring the Colony under the thumb of a Presbyterian Parliament, to impose the Solemn League and Covenant upon all its inhabitants, and to procure the establishment of the (Presbyterian) Church of England as a state church." [2]

There is little reference to venereal disease in the colonial literature of the period, and in New England such diseases were undoubtedly rare because of the "stern morality" of the people and because of the severe punishment meted out to those who were discovered in sexual irregularities.

It is also probable that the few who suffered from such afflictions would postpone as long as possible the disclosure of their disease to the physician who was also their pastor, and whose "pious converse"

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1. Thatcher, James: American Medical Biography **1**:14, 1828.

2. Kittredge, G. L.: Doctor Robert Child the Remonstrant. Reprinted from the Publications of the Colonial Society of Massachusetts, Cambridge **21**:1919.

might be especially unwelcome at such a time. And what would be the plight of an erring youth when, as in the case of John Wilson of Medfield, the pastor, schoolmaster and physician was one and the same person? This good physician was the son of the minister of Boston, of the same name, of whom it was said that he was a man "than whom orthodoxy in New England had no champion more cruel and ungenerous, and whose zeal and passion led him to revile and even strike prisoners being led away from the judgment seat," and who vociferated in his pulpit that "he would carry fire in one hand and faggotts in the other to burn all the Quakers in the world." [3]

FIRST KNOWN OUTBREAK OF SYPHILIS IN NEW ENGLAND

The first known outbreak of syphilis in New England occurred in 1646, and is described at length in the "Diary of John Winthrop." Though it has often been quoted, it is curious enough to bear an occasional repetition. Preceding the description by a few pages, is the following entry:

> October, 1645. At Ipswich there was a calf brought forth with one head, and three mouths, three noses and six eyes. What these prodigies portended the Lord only knows, and in his due time he will manifest.[4]

The writer does not state that the omen referred to the outbreak of syphilis, but that is the first calamity recorded in his diary.

> There fell out also a loathsome disease at Boston, which raised a scandal upon the town and country, though without just cause. One of the town ——— having gone cooper in a ship into ———, at his return his wife was infected with lues venerea,[5] which appeared thus: Being delivered of a child, and nothing then appearing, but the midwife, a skilful woman, finding her body as sound as any other, after her delivery, she had a sore breast, whereupon divers neighbors resorting to her, some of them drew her breast, and others suffered their children to draw her, and others let her child suck them (no such disease being suspected by any), by occasion whereof about sixteen persons, men, women and children, were infected, whereby it came at length to be discovered by such in the town as had skill in physick and surgery, but there was not any in the country who had been practised in that cure. But

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3. Adams, Brooks: The Emancipation of Massachusetts, 1887, p. 135.

4. Winthrop, John: The History of New England from 1630 to 1649, edited by James Savage, Boston **1**:254, 1826.

5. Savage, the editor, adds the following in a footnote: "The first two blanks in this paragraph were once filled, the first probably with the person's name, the second with that of the place, but they have been effectually erased. In such an important narrative it may be of little consequence that it was first written, the man "infected his wife, and leaving her with child went to sea again; the woman knew all, but not what she ailed. So that reports were various. Whether the result, as stated in the text, be the truth or not it is of less consequence than to observe, how the ignorance of our fathers on this topick gives confirmation to the general opinion of their blameless manners."

> (see the good providence of God) at that very season there came by accident a young surgeon out of the West Indies, who had had experience of the right way of the cure of the disease. He took them in hand, and through the Lord's blessing recovered them all ——— in a short time. And it was observed that although many did eat and drink and lodge in bed with those who were infected and had sores, etc., yet none took it of them, but by copulation or sucking. It was very doubtful how the disease came at first. The magistrates examined the husband and wife, but could find no dishonesty in either, nor probable occasion how they should take it by any other (and the husband was found to be free of it). So it was concluded by some that the woman was infected by the mixture of so many spirits of men and women as drew her breast (for so it began). But this is a question to be decided by physicians.[6]

It seems probable that Dr. Child made use of this outbreak of syphilis in his Remonstrance, which was made about the same time, for in it is found the statement that the "hand of our good God . . . seems to be against us. . . . Yea at this time laying his just hand upon our familyes, taking away many to Himself, striking others with unwonted malignant sickness, and some with shameful diseases."[7]

TREATMENT OF SYPHILIS IN COLONIES

The search for remedies for syphilis among the plants of the New World began almost with its discovery. Guaiac was the most celebrated drug found there. Its virtues were widely heralded, and Fracastor sung of it as follows: The place on

> which the Spanish navigators were the first to land . . . they called Hispaniola (Hayti). This land is sown with gold; but that which makes a greater wealth for it than gold is the precious tree to which the natives of the country have given the name of Guaiac. . . . And Diana, O Prodigy, has not completed her career when the action of the remedy is already revealed. The pustules dry, the ulcers heal, the pains disappear, and the flower of youth is born again with the return of health.

Many herbs and roots were tried in early Colonial days for syphilis as well as for other diseases. Some were shown to the colonists by the Indians, and native medicines were a necessity, the distance from England and the isolation of the small settlements making a sure supply of medicines impossible. One or two examples of the treatment used for syphilis may be of interest.

A popular medical book, which ran through several editions about 1730, entitled "Every Man His Own Doctor or The Poor Planter's Physician. Prescribing Plain and Easy Means for Persons to Cure

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[6] Winthrop, John: The History of New England from 1630 to 1649, edited by James Savage, Boston **1**:257, 1826.

[7] Hutchinson Papers, Albany, p. 215.

Themselves of All, or Most of the Distempers, Incident to This Climate, and with very Little Charge, the Medicines Being Chiefly of the Growth and Production of This Country," gives the following description of syphilis and its treatment, which is the same as that prescribed for yaws:

> The Pox may be cured exactly in the same Manner: And because the Symptoms are much the same, it is very probable, the one was a Graft of the other (i. e., Yaws). The pious *Spaniards* catch'd it from their *Negro* Mistresses in the *West-Indies,* and had the Honour of propagating it from thence to all the rest of the World.
>
> In both cases, confine yourself altogether from eating Flesh, from a strong Drink, and be very careful of catching Cold.
>
> To avoid these Misfortunes, eat seldom of fresh Pork which breeds very gross Humours; live not too near a Swamp; not ever venture upon strange Women, especially upon Ethiopians.

So much for etiology and prophylaxis. The treatment is described as follows:

> Take 1 Ounce of the Bark of *Sumac Root,* 1 Ounce of the *inner Bark of Pine,* and 2 Ounces of the Bark of *Spanish Oak;* boil these together in 2 Quarts of *Water* 'til the *Decoction* be very strong. Of this Liquor drink a full Pint, Milk-Warm, and immediately after it, Half a Pint, quite cold: and it will give you a powerful Vomit.
>
> The next Morning, take Half a Pint of the same *Drink* warm, and the same Quantity again in the Evening; and continue to doing, for 6 Weeks, or 2 Months; only the *Vomit* must be repeated every seventh Day. In the mean Time, gargle your Throat, and wash all your Sores and Ulcers with the same warm Liquor, which ought to be made fresh every 2 Days. Beside all this, you must chew the *Sumac* Root very often, and swallow the healing juice.
>
> Every Night, before you go to Rest, take 2 *Pills,* made of *Turpentine* and *Deers Dung* in equal Quantities.[8]

Another treatment is of special interest because it was introduced by John Bartram, the botanist. Bartram, who with Benjamin Franklin, was one of the founders of the American Philosophical Society, was not a physician, but he had a penchant for medical matters "and he even acquired so much knowledge of the latter science, as to be very useful: and in many instances he gave great relief to his poor neighbors, who were unable to apply for medicines and assistance to the physicians of the city" (Philadelphia).[9]

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[8] Everyman His Own Doctor or The Poor Planter's Physician. Ed. 2, Williamsburg and Annapolis, William Parks, 1734, p. 50. (A third edition was printed in the same year by B. Franklin. The book has been attributed to John Tennant.)

[9] Darlington, William: Memorials of John Bartram and Humphrey Marshall, 1849, p. 38.

Lobelia is the plant he described for use in syphilis. This description is found in a pamphlet published as an appendix to Short's Medicina Brittanica, an American edition of which was edited by Bartram, and published in Philadelphia in 1751 by B. Franklin and D. Hall Few copies of the pamphlet are now to be found. It is entitled: "Mr. Bartram's Appendix: containing *Descriptions, Virtues* and *Uses* of sundry Plants of These Northern Parts of *America;* and Particularly of the Newly Discovered *Indian* Cure for the *Venereal Disease.*" The book contains this description:

> *Lobelia.* This curious Plant riseth from a fibrous Root to three or four Feet high, with a Spike of Blue Flowers surrounding the Stalk for near a Foot in Length: It grows in rich shady Ground; it is a scarce Plant in many Parts of the Country.
>
> The learned *Peter Kalm* (who gained the Knowledge of it from Colonel *Johnson,* who learned it from the *Indians,* who, after great Rewards bestowed on several of them, revealed the Secret to him) saith, That the Roots of this Plant cureth the *Pox* much more perfectly and easily than any mercurial preparations, and is generally used by the *Canada Indians,* for the Cure of themselves, and the *French* that trade amongst them, tho' deeply infected with it. They take a Handful of the Roots, and boil them in a Quart of Water, and drink the Decoction, beginning with Half a Pint at first, if the Patient be weak, then increase the Dose every Day as he can bear its purging; but if he can't bear it every Day, let him omit it a Day or two, then take to it again, as he finds Occasion, until he is cured: They wash the Ulcer with the Decoction; but if it be deep and rotten, they put some Powder of the inner Bark of the Spruce-tree into it, which helps to dry it up, but if the Disease is inveterate, they drink the Decoction of *Ranunculus Folio Reniformis.* An old *Sachem* told Colonel *Johnson* of another Shrub, with a red Root, from which proceeds several slender Branches, eighteen Inches or two Feet long, on which grow Spikes of white Flowers, which produce three-square black Seed-Pods; the leaves some of our People drink as Tea, and some smoak it with Tobacco; the Roots of this, bruised and boiled, and the Decoction drank, the *Sachem* said, he rather preferred to the *Lobelia;* but the *Lobelia* seems to be of the most general Use, and with extraordinary Success.
>
> *More particular Directions how to use the Lobelia-Root for the Venereal Disorder, obtained from the Indians, by Col. J.*
>
> "After making a Decoction of it, the Patient is to drink about two Gills of it very early in the Morning, fasting, the same before Dinner, and Bedtime. Add or diminish as you find it agree with the Patient's Condition: The third Day begin Bathing, and continue it twice a Day, untl the Sores are well cleansed, and partly healed, then use the Lotion but once a Day till quite well; observing all the Time to use a slender Diet (vegetable Food, and small Drink) as in other Courses of Physick, a Salivation excepted. These are the Directions I have had from the Person who gave me the Secret."[10]

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[10] Short, Thomas: Medicina Brittanica, Ed. 3, Reprinted, Philadelphia, 1751, B. Franklin and D. Hall. Appendix by John Bartram. Mr. Bartram's Appendix: containing descriptions, virtues and uses of sundry plants of these northern parts of America; and particularly of the newly discovered Indian Cure for the Venereal Disease, p. 5.

News and Comment

A NEW JOURNAL OF DERMATOLOGY

"Ceska' Dermatologie" is the name of a new journal recently founded in Prague. The first number appeared October, 1919, and is dedicated to Professor Janowsky. The managing editors are Prof. F. Samberger and Priv. Doz. Dr. A. Tryb. The journal is issued in the Czeck language, is a monthly, and is devoted to dermatology and venereal diseases.

Abstracts from Current Literature

EXPERIMENTAL STUDIES ON THE INVESTIGATION OF THE NATURE OF THE ANAPHYLACTOID CONDITION CAUSED BY THE REPEATED INTRAVENOUS INJECTION OF ARSPHENAMIN. Norimasa Hirano, Kitasato Arch. Int. Med. **2**: (April) 1919.

After discussing the symptoms and various theories concerning the causation of this dreaded reaction, Hirano mentions Milan's work which he thinks gives a clue to the cause. In this work is mentioned that the previous administration of epinephrin has successfully prevented the development of an anaphylactoid condition in a patient who used to manifest the phenomenon. Hirano also mentions the fact that the development of this condition was successfully prevented by administering a dose of arsphenamin in two portions, a smaller portion to be injected one hour before the larger portion. From these facts the author was led to believe that there may exist some intimate relation between arsphenamin and the suprarenal systems in the development of the anaphylactoid state.

To this end Hirano made several experiments on rabbits: 1. An experiment to ascertain the change of the chromaffin substances in the suprarenal glands caused by the injection of arsphenamin.

Various quantities of arsaminol and neo-arsaminol were injected into healthy rabbits. The dose ranged from 0.007 to 0.7 gm. per kilo body weight. After various intervals the rabbits were killed or bled to death. The suprarenal glands were then extirpated and the chromaffin reaction was determined. It was found that if a large amount of arsphenamin was injected (0.8-0.07 per gram kilo weight), the chromaffin reaction was very weak one hour after the injection; but if a small quantity, for example, a therapeutic dose was used, the reaction was produced in a widely differing intensity which was sometimes difficult to distinguish from that exhibited in the control.

2. An experiment to ascertain epinephrin contents of the bilateral suprarenal glands after injection of arsphenamin and neo-arsphenamin.

For this experiment, the epinephrin content of the bilateral suprarenal glands of normal rabbits was first determined, and was found to be on the average 0.2 gm. Five rabbits then received injections of arsphenamin in large quantities, 0.06-0.07 gm. per kilo weight. They were killed one hour after the injection. There was a remarkable decrease of the epinephrin contents in these rabbits, the average being 0.116 gm. Hirano then determined the influence of arsphenamin on the epinephrin contents, when arsphenamin was injected in therapeutic amounts. He wished to determine whether the epinephrin contents decreased in quantity and if so, how long it took before the normal content was regained.

More than ten rabbits were injected with from 0.001 to 0.03 gm. of arsphenamin per kilo weight. The animals were killed from one to four hours after the injection, and it was found that the epinephrin contents diminished in amount, not only in therapeutic dose. They even were decreased by so small a quantity as from 0.002-0.003 gm. per kilogram. By the injection of smaller doses, such as 0.001 gm. per kilogram weight, no decrease was effected. With reference to the decrease of the epinephrin contents and the final return to normal, after an injection of arsphenamin, Hirano found that the decrease reached its minimum in six hours from the time of injection of a large quantity of arsphenamin, i. e., 0.06 gm. per kilogram. It then gradually regained its former state. The recovery was nearly complete in from ten to twenty-four hours and complete in forty-eight hours.

With reference to neo-arsphenamin, Hirano found that the epinephrin content of both suprarenals decreased but that the amount was normal in two hours. The maximum therapeutic dose of neo-arsphenamin did not produce any decrease in the epinephrin contents of the suprarenals.

3. Investigation of the Causes of the Decrease of the Epinephrin Contents of the Bilateral Suprarenal Glands after the Intravenous Injection of Arsenic Compounds: These tests were carried out after the Trendelenburg's method and after what the author calls the frog perfusion test.

A rabbit was injected with 7 c.c. of a 1:200 arsphenamin solution or 0.02 gm. per kilogram body weight. Blood was withdrawn just before, immediately after and one hour after the intravenous injection of arsphenamin. The serum prepared from blood withdrawn immediately after an injection of arsphenamin did not produce as remarkable a change in the number of drops as did the serum taken before the injection of arsphenamin. The serum, one hour after the arsphenamin injection, also produced a similar result as the one immediately after the injection. From this Hirano concludes that the epinephrin contents of the serum immediately after and one hour after the injection of arsphenamin were less than those of normal blood. The experiment was repeated in different rabbits and the serum to be tested was taken before, immediately after, two hours, and two and a half hours after the injection of arsphenamin. The experiment showed that the number of drops will decrease by the perfusion of untreated serum, but that it will return to the former state in about thirty minutes. The change produced by the perfusion of the serum that is prepared from blood withdrawn immediately after injection will be repaired in the course of eighteen minutes. The decrease in the number of drops that was produced by the perfusion of the serum taken immediately after the injection of arsphenamin was not so great as the one obtained with untreated serum. The decrease of the number of drops by the perfusion of the serum that was prepared from blood withdrawn after two and a half hours was most remarkable. The change was noted in the course of more than one hour after the perfusion.

Hirano concludes from these experiments that "a remarkable decrease in the number of drops resulted from the perfusion of the serum prepared with the blood of an animal that had not yet received any intravenous injection of arsenic compounds, or the normal serum. By perfusion of the serum treated with arsenic a far less remarkable decrease was, however, produced, and the repair of the change in the drop-frequency, moreover, was seen to take place sooner. This decrease of the drop frequency was far more remarkable by the perfusion test made with the serum that had been prepared after from 2 to 2½ hours from the intravenous administration of arsenic, than was the case with normal serum. Thus it will be seen that the epinephrin-like substance contained in the blood serum is diminished in quantity immediately after the intravenous infusion of 0.02 gm. per kilogram body weight of arsphenamin, but that it increases after the lapse of two or two and a half hours after the injection. Another series of tests made with 0.03 gm. of arsphenamin per kilogram body weight brought about nearly the same results. The change in the number of drops by perfusion test made with the blood plasma was not so manifest as with blood serum.

The increase or decrease of the vasocontractile substance in blood serum does not prove the increase or decrease of the epinephrin contents of the circulating blood from which the serum has been prepared. But, considering the fact that arsenics have been proved to interrupt the epinephrin-sublimate reaction in vitro, the introduction of arsenics into the circulating blood by means of intravenous injection may play a part in the decrease of epinephrin in the same blood.

The increase of the epinephrin-like substance that is brought about after a lapse of two or two and a half hours after intravenous injection of arsenic compounds may partly be interpreted by the assumption that the decrease of epinephrin in the circulating blood may result in the invigoration of the function of the suprarenal systems, and especially of the suprarenal glands, in order to compensate the deficiency of the blood constituents. The change in the quantity of epinephrin-like substance in blood serum, however, may not be fully explained by this assumption, because we are as yet left in ignorance regarding the nature and the function of the epinephrin-like substance found in the circulating blood. It may be conjectured, however, that this substance would be produced from some preexisting mother substance in the blood by coagulation, and that this preexisting mother substance must have been destroyed by arsenic compounds introduced into the circulating blood, but that afterward it must have been increased by compensatory production from the suprarenal systems.

Hirano concludes from the above experiments that the decrease of the epinephrin contents of the suprarenal glands may be explained by the assumption that some part of the arsenic compounds introduced into the circulating blood may find its way to the suprarenal glands and there combine with the epinephrin, while the remaining part may lead to the immediate decrease of epinephrin in the circulating blood, which process may excite the splanchnic nerve and cause an invigorated secretion of epinephrin from the suprarenal glands in order to compensate the deficit in the blood.

Hirano then conducted experiments to determine the changes that take place in the suprarenal glands after repeated intravenous injections of arsphenamin or neo-arsphenamin, and found that the epinephrin contents of the suprarenal glands of rabbits after three intravenous injections of 0.02 gm. per kilogram weight, given once a week, were sometimes increased. Even when a therapeutic dose of arsphenamin is given to the animal thus treated, no remarkable decrease of the epinephrin contents of the suprarenal glands is observable. On the contrary, when a rabbit is given an intravenous injection of 0.03 gm. per kilo body weight for three weeks, the epinephrin contents of the suprarenal glands are the same as those of normal rabbits. But if a therapeutic dose of neo-arsphenamin is given to an animal thus treated, a remarkable decrease of the epinephrin contents of the suprarenal glands is observed.

Gutierrez, Manila.

UEBER DIE VANADIUMTHERAPIE BEI SYPHILIS (CONCERNING VANADIUM THERAPY IN SYPHILIS). Ferdinand Winkler, Dermat. Wchnschr. **70**:147 (March 6) 1920.

"If one injects a cubic centimeter of a 2 per cent. solution of sodium vanadate into a primary lesion of syphilis in such a manner that a part of the fluid infiltrates the sclerotic tissue and a part infiltrates a zone surrounding the entire lesion, a characteristic retrogression of the syphilitic granuloma is to be noted as early as the next day; the indurated wall or border becomes smaller and the characteristic color of the efflorescence wanes; smear preparations show only disintegrated particles of spirochetes and the dark-field examination is negative.

"Should this local injection be repeated during the following three to four days, the sclerosed part heals, skin forms over the lesion and the induration of the tissue disappears.

"Likewise the results with broad condyloma when similarly treated locally are those of apparent healing. There is a corresponding repair of the syphilitic tissue and a disappearance of the spirochetes from the tissue juices. This healing, however, is more gradual, and more local injections are necessary than with the above lesions."

If one injects sodium vanadate into a syphilitic inguinal gland, the response in many cases is a swelling followed by a rapid healing. Frequently, however, there is a resorption of the gland proliferation without the intervening swelling. Whereas, before the sodium vanadate injection the gland will yield on aspiration material rich in spirochetes, soon after the injection the aspirated material shows great diminution in the number of spirochetes.

"In rebellious cases of indurative edema, vanadium injection into the edematous tissue frequently brings about rapid improvement. Moreover, local vanadium therapy favorably influences the syphilitic lymph channels.

"Sclerotic rests, such as one not seldom sees for some time after the outbreak of exanthemas, rapidly diminish under the influence of local vanadium injections. Disintegrating gummas face about under this treatment, the necrotic mass disappears, leaving a well-healed scar. Fissures of the folds of the mouth also quickly heal."

Scaling syphilids of palms and soles react favorably under this local treatment. Macular forms, on the other hand, are not appreciably influenced by vanadium therapy. Leukoplakia of the mouth mucous membrane shows no appreciable improvement with vanadium therapy.

"The basis of vanadium therapy in syphilis depends on the great toxicity of vanadium for the spirochetes."

This action of vanadium on spirochetes and trypanosomes has been proved experimentally in great detail by Proescher and Seil (*Am. J. Syphilis* **1:** No. 2 [April] 1917).

This toxic action in all probability depends on the high oxidation properties of vanadium salts, especially in conditions where vanadinic acid (HVO_3) is an intermediate product.

The pharmacologic and the toxicologic action of various vanadium salts is discussed. The work of various authors is cited. Vanadium pentoxid and ammonium metavanadate are the most toxic of the salts of vanadium which have been tested. Sodium hexavanadate and vanadyl sulphate, on the other hand, are the least toxic. The salts of pyrovanadinic acid are less toxic than those of orthovanadinic acid, and the latter in turn are less toxic than those of metavanadinic acid.

Toxicity is manifested in animals by circulatory disturbances, failing respiration, disturbance of the heat regulation center and coma. There may be albuminuria, cylindruria and finally anuria. There is increased intestinal peristalsis and bloody diarrhea and congestion of the lung and portal vessels.

In man the intravenous injection of sodium tetravanadate (in quantity corresponding to 20 mg. (V_2O_5) has resulted in lacrimation, depression of the pulse, incontinence of feces, irregular frequent respiration and a lowering of the temperature 3 C. Other symptoms that have appeared are dry bloody cough, loss of appetite, anemia and nervous disturbances. Postmortem sections show definite and widespread pathologic change. The toxic dose of sodium tetravanadate in man (according to Proescher and Seil) corresponds to about 20 mg. of V_2O_5 when injected intravenously. This quantity is well tolerated when injected subcutaneously or intramuscularly.

Helouis and Delarue have employed small doses of vanadium salts as a stimulus of the appetite and to improve the general condition in tuberculosis. Various other French authors have reported favorably on the use of various vanadium salts as alteratives. The body, however, quickly acquires a tolerance and frequent periods of rest from the drug is advised. Vanadium has been used in anemia, chlorosis, tuberculosis, diabetes, neurasthenia, acute and chronic rheumatism and in various nutritional disturbances.

As a germicidal agent vanadium salts have no value. Streptococci, meningococci and the bacilli of diphtheria, tetanus, edema, typhus, dysentery and enteritis withstand from 0.2 per cent. to 0.8 per cent. solutions from two to eight days. Tubercle bacilli were still viable after being in a 5 per cent. solution of sodium tetravanadate for four weeks. *Trypanosoma Brucei,* in contrast to *Trypanosoma equiperdum,* are soon destroyed by vanadium salts.

Experimentally with guinea-pig syphilis, vanadium salts seem to possess a specific action against spirochetes. In experimental lesions of the testicles the spirochetes are quickly destroyed and the lesions heal.

The experimental work of A. W. Stillians (Chicago) is commented on. Stillians reports the largest series of cases (thirty-two) in which vanadium therapy has been tested. The syphilitic lesions soon disappeared in each case and the dark-field examinations speedily became negative. Stillians reports, however, that in none of the cases treated exclusively by vanadium therapy did the Wassermann reaction become negative.

The author advocates vanadium therapy in early syphilis and as an adjunct to arsphenamin therapy.

Elbert Clark, Chicago

EXPERIMENTAL SYPHILIS IN THE RABBIT. I. Primary Infection in the Testicle. Wade H. Brown and Louise Pearce, J. Exper. Med. **31**:475 (April) 1920.

Using two strains of *Spirochaeta pallida,* all rabbits used were infected after an incubation period of from two to six weeks.

The testicular reactions were of two fundamental types: one in which the reaction was intense with acute exudation and infiltration to be followed by subsequent recurrences; the other types being more chronic and consisting largely of infiltration and proliferation. A third group tended to combine the characteristics of both of the others. The duration of the testicular process varied from four weeks to six months, being, in general, inversely proportional to the intensity of the local reaction.

EXPERIMENTAL SYPHILIS IN THE RABBIT. II. Primary Infection in the Scrotum. Part I. Reaction to Infection. Wade H. Brown and Louise Pearce, J. Exper. Med. **31**:709 (June) 1920.

Animals with thin and delicate scrotal skin were selected for this work, the inoculation being made by implanting a small piece of infected testicle or granulomatous skin nodule in a pouch prepared in the scrotum. The specific reaction is the same by all methods of scrotal inoculation. In the use of a virus emulsion the incubation period varied from one to four weeks, the initial reaction in the scrotum appearing in one of three general forms: (1) small circumscribed swellings or diffusely spreading patches of a rose-pink color situated in the papillary and reticular layers of the skin, being gelatinous in character and frequently associated with a rich vascular network; (2) a minute, translucent nodule or indurated plaque in the papillary layer more superficial than the first, and (3) an opaque, porcelain-white nodule of extreme hardness in the depths of the scrotum. The first two were the most frequent and earliest.

The development of the chancres was marked by an extension of the reaction, spreading diffusely through the scrotum. The various types are described in detail.

The incubation period for tissue implants and virus inoculation was much the same although the reaction following implants must be regarded as partly wound healing, partly foreign body reaction and partly specific. The later development of the chancres was influenced by various degrees of edema, congestion, irregularities in granulation process and acute inflammatory reaction.

Part 2. Scrotal Lesions and the Character of the Scrotal Infection, p. 729.

Typical scrotal chancres are divided into nodular and lenticular or discoid varieties, depending on the part of the scrotum in which they develop and also on the mode and rate of development. The nodular type was also divided into two groups—one with moderate necrosis and ulceration, the other with slight ulceration or none.

The course of the infection appeared to be about the same as it is when the testicle is infected, although subject to great variations individually. The scrotal lesions disappeared spontaneously after a period varying from a few weeks to months.

EXPERIMENTAL SYPHILIS IN THE RABBIT. III. Local Dissemination, Local Recurrence and Involvement of Regional Lymphatics. Wade H. Brown and Louise Pearce, J. Exper. Med. **31**: 749 (June) 1920.

Three general types of local reaction were recognized in this work: (1) a diffuse reaction with the formation of multiple foci of secondary reaction arising subsequent to the development of the primary lesion; (2) a reaction characterized by the formation of lesions having a perivascular arrangement, and (3) dissemination of the infection with the production of multiple lesions showing no demonstrable connection with the primary focus of infection.

Recurrent lesions were identical in all respects, whether the primary lesion had healed spontaneously or had been assisted by artificial means.

A regional adenopathy always follows the initial lesion although there may be no lesions to indicate this dissemination. An examination of the inguinal glands shows, however, that they are involved shortly after inoculation and that a pallidum reaction may be detected there before a scrotal infection is recognized.

Jamieson, Detroit.

PARAPLEGIA AFTER ARSPHENAMIN. T. J. Dimitry, J. A. M. A. **74**:1150 (April 24) 1920.

Dimitry reports an interesting case of a man who suffered a complete loss of sight before any other symptoms developed to make possible a diagnosis, though some precursory symptoms obtained in his history were not recognized at the time as being important. Fundus examination elicited a distinct elevation of the optic nerve of both eyes. This elevation was greater in the right eye. The pupils were widely dilated and did not respond to light. Tests for syphilis were negative. Following the intravenous injection of 0.06 gm. of arsphenamin, the patient complained of stiffness in the legs and pain in the back. He could not move his right leg and during the afternoon this paralysis extended to the other leg. It was necessary to catheterize the bladder and later to contend with an overflow of the urine. He suffered an inability to evacuate the bowels, and subsequently an incontinence of feces. He developed decubitus and a painful hyperesthetic area of the left arm. The paralysis of the legs was absolute, and all voluntary motion and sensation in all its qualities, including temperature and touch, was destroyed. Varying degrees of deep and superficial anesthesia and hyperesthesia extended to within an inch of the nipple anteriorly, and not quite so high posteriorly. The reflexes were abolished in the legs with a flaccid paralysis and the appearance of a rapid wasting. Two days after the injection of arsphenamin, the elevation in the optic nerve had improved and within the next day had disappeared entirely, leaving a normal appearing optic nerve, though the patient was blind. In spite of the apparently harmful effect of the arsphenamin, a second dose of 0.06 gm. of arsphenamin was given, and a dose of 0.09 gm. of neo-arsphenamin was given a few days afterward. Mercury was used by inunctions and the iodids were used in increasing doses, and for weeks the patient received 75 drops of saturated solution of potassium iodid three times a day. Seven months later the patient could walk and had practically perfect vision. There remained some bladder disturbance. Though the Wassermann test was negative both for the blood and for the spinal fluid, the other tests showed that the etiology was that of syphilis. Dimitry urges that it is well to remember that syphilis presents a vagary of symptoms at times, lacking a definite explanation. What appears as an incongruous syndrome both pathologically and clinically is often made clear when syphilis is taken into consideration and an appreciation of the changes that might occur from a syphilitic arteritis, better known as a Huebner arteritis.

Waugh, Chicago.

FURTHER EXPERIENCE WITH SODIUM GYNOCARPATE (SODIUM GYNOCARDATE "A") AND A TRIAL OF SODIUM MORRHUATE IN LEPROSY. Sir Leonard Rogers. WITH NOTES OF CASES BY Jogesph Chandra Mukerjee, Indian M. Gaz. **54**:165 (May) 1919.

Rogers believes that the more effective higher melting point preparations consist chiefly of hydnocarpic (melting point 59-61) and chaulmoogric (melting point 68) acids with sufficient of the lower melting point preparations to make the salts soluble in water. Basing his belief on the results of his experiments, Rogers found the sodium salt of hydnocarpic acid most active in leprosy. He treated a series of cases with a preparation made of Hydnocarpus wightiana oil, consisting mainly of sodium hydnocarpate with sufficient of the lower melting-point acids to make it soluble, and also containing a little sodium chaulmoograte. The melting point of the mixture of fatty acids is approximately 48 C., and Rogers found the products obtained from cheaper and more easily obtainable hydnocarpus oil at least as efficient in leprosy as that obtained from true chaulmoogra oil.

Rogers treated fourteen cases with this mixture. The disease was present in different forms, tubercular and mixed types. The duration of the disease was from six months to fifteen years with an average duration of 3.4 years. The dose given ranged from 0.5 c.c. to 5 c.c. of a 3 per cent. solution. The duration of the treatment is from six months to fourteen and one-half months, the average duration being eight and one-tenth months. The results obtained were: slightly improved, 1; much improved, 6; lesions disappeared, 7.

Rogers reviews also the cases treated with sodium gynocardate (hydnocarpate) reported in the *Indian Journal of Medical Research,* vol. 5, October, 1917, and reports the present condition. Of fourteen patients who were not lost sight of or died of intercurrent diseases, five have remained well for over a year, and two more for shorter periods; two advanced cases remain greatly improved and one slightly improved; one showed no improvement and three have had relapses. All of the patients were in an advanced state, and Rogers thinks that the results obtained are highly encouraging.

Febrile Reactions after Sodium Hydnocarpate: Rogers believes that milder reactions are beneficial to the patient. Microscopic examinations have shown that the softening and shrinking of tubercular lesions of leprosy under the influence of sodium hydnocarpate intravenously is regularly accompanied by breaking up of the lepra bacilli until either only a minute red spot remains, or they disappear. This may occur without any febrile or local reactions being observed, but more rapidly when mild reactions take place. The fever, Rogers believes, is due as in the case of tuberculosis, to the liberations of toxins consequent to the breaking up of the organisms. The fever may be so great and prolonged as to temporarily break down the resisting power of the patient, and even cause the spread of the disease for a time. This is specially true in greatly thickened tissues so that especial caution is necessary in increasing the dosage.

Rogers cannot predict a complete cure and complete eradication of the lepra bacilli from the system on account of the relapses reported, but he thinks the results already obtained are sufficiently encouraging to stimulate further work along these lines.

Part II. Sodium Morrhuate in Leprosy.—This is prepared from cod liver oil, and is found to have the great advantage over sodium hydnocarpate of producing little pain or induration on subcutaneous injections. Sodium morrhuate can also be injected intravenously and is far less irritating to the veins than sodium hydnocarpate. Although Rogers cannot draw definite conclusions, owing to the short time that the drug has been used, he believes it to be a very active drug in the treatment of leprosy.

He concludes with this important observation: "that the breaking up and eventual disappearance of the bacilli and good progress in leprosy under sodium morrhuate show that there is nothing absolutely specific against leprosy in chaulmoogra oil products, so other unsaturated fatty acids may also be expected to yield effective preparations against acid-fast bacilli of both leprosy and tuberculosis. Nor is such action, as far as we yet know, limited to the resistant acid fast bacilli, and thus a vast field of research is opened up."

Gutierrez, Manila.

GRANULOMA INGUINALE. Douglas Symmers and Albert D. Frost, J. A. M. A. **74**:1304 (May 8) 1920.

The authors have recently had occasion to study two chronic ulcerative lesions of the groin occurring in negroes. Since in the tropics, there are many granulomatous formations about which little is known, it is impossible at present to state with certainty whether the various chronic ulcerative lesions occurring in the region of the groin and external genitals are manifestations of one and the same process or anatomically related reactions arising in response to different causative agents, or the result of combined factors. However this may be, there is at least one variety of granuloma inguinale that has been frequently observed and whose clinical features appear to be much the same, no matter in what country they are seen. In this particular variety, cell inclusions were described by Donovan in 1905 and have since been found in ulcerative lesions of the groin in widely remote parts of the world. These intracellular inclusions have been studied by Walker, who regards them as small encapsulated bacilli belonging to the Friedländer group. The evidence that they bear a causative relationship to granuloma inguinale, however, appears not to have been definitely established. On the other hand, it has been suggested that the presence of these intracellular bodies is due to secondary infection of venereal or other pudendal lesions and that, once established in the tissues, they dominate the local pathologic process and promote destruction of tissue. In the secretions in both the cases reported, intracellular bodies morphologically identical with those described by Donovan were found. One of the cases appeared to represent a typical example of granuloma inguinale as encountered in various parts of the tropics. The other, however, was possibly syphilitic in nature.

Waugh, Chicago.

SUPPLEMENTARY REPORT ON THE TREATMENT OF LEPERS WITH GYNOCARDATE OF SODA "A." E. Muir, Indian M. Gaz. **54**:130 (April) 1919.

This report is supplementary to a report on the treatment of thirty lepers which appeared in the June, 1918, number of the *Indian Medical Gazette*. Muir reports in detail the thirty cases previously reported, and compares the action of sodium gynocardate and sodium morrhuate. He also reports twenty-three new cases treated by either or both drugs.

He concludes that:

1. Sodium gynocardate is slightly more rapid in its action on anesthetic areas, but that the nodular patches made equally rapid progress. Sodium gynocardate "A" has led to the destruction of the veins in several cases and it was found necessary to give sodium morrhuate. He therefore recommends the following system of dosage in order to obtain the maximum effect: First Week: (1) sodium gynocardate "A" 0.5 c.c. intravenously on the first day; (2) sodium gynocardate "A" 0.5 c.c. to 0.25 c.c. intravenously on the third day; (3) sodium morrhuate 0.5 c.c. intramuscularly on the fifth day.

In this way the dosage should be increased by 0.5 c.c. week by week up to 5 c.c., provided there be no marked febrile reaction or other danger signal. When there is a marked febrile reaction the dose should be halved and again gradually raised, but kept at least 1 c.c. below the dose that produced the marked reaction.

2. In some cases over-dosage led to a marked febrile reaction accompanied by the formation of pustules, and later of sores on the limbs followed by a recrudescence of the anesthesia.

3. In one case there was almost complete recovery but the treatment was stopped too soon and this was followed by a recrudescence of the anesthetic areas.

4. Rapid progress was made at first in several cases followed by slower but steady progress toward recovery. The anesthesia of the face and of the trunk recovered first.

5. Early cases, especially in children, healed up rapidly with intravenous injections of sodium gynocardate "A."

6. As to the length of treatment, the author cannot advise definitely. He thinks, however, that the injections should be continued for some months after the symptoms have entirely disappeared.

GUTIERREZ, Manila.

ARSPHENAMIN AND NEO-ARSPHENAMIN. WILLIAM A. SMITH, J. Lab. & Clin Med. **5**:518 (May) 1920.

In this general article Smith discusses the origin, present supply, rules for manufacture, chemistry, physical properties, technic of administration, reactions and their causes, use in therapeutics and relative value of arsphenamin and neo-arsphenamin. As the supply and rules for manufacture in America are not generally known, the following information should be of interest:

During the war, shipments were stopped, and the supply in the United States was exhausted in 1915. Patent protection was withdrawn in the allied countries, and firms in England, France, Japan and Canada began to manufacture these compounds. After the United States entered the war, the Adamson Bill was passed, granting citizens the right to operate patents owned by enemy aliens. The result was that several products were placed on the market, varying both in their chemical and their physiologic properties. It became necessary to exercise precaution in granting licenses to manufacture these products; for this reason the U. S. Public Health Service defined the properties of good preparations, and the Federal Trade Commission formulated rules and toxicity tests which must be complied with, or the license of the manufacturer may be revoked. The firms licensed at present are:

The Dermatological Research Laboratories, Philadelphia Polyclinic, whose products are called arsphenamin and neo-arsphenamin.

The Takamine Laboratory Co., Inc., New York City, whose products are called arsaminol and neo-arsaminol.

The Farbwerke-Hoechst Co., New York City (at H. A. Metz Laboratories Inc.), whose products are called salvarsan and neosalvarsan.

The Diarsenol Co., Buffalo (Synthetic Drug Co., Toronto), whose products are known as diarsenol and neodiarsenol.

The product of the Dermatological Research Laboratory was known as arsenobenzol, and was found to be identical with salvarsan in composition and equal to it therapeutically, by the Council on Pharmacy and Chemistry of the American Medical Association. This product was made under the direction of Dr. Schamberg, and was first made in this country.

On March 4, 1918, the Federal Trade Commission adopted certain rules for the manufacture of these products; chief among these are:

1. These products are to be named and labeled arsphenamin and neo-arsphenamin, respectively. (Arsphenamin was also previously called arsphenolamin hydrochlorid.)

2. The products are to be sold only in colorless glass ampules, containing an atmosphere of an inert gas.

3. The arsenic content of arsphenamin must be between 29.5 and 31.57 per cent.

4. The arsenic content of neo-arsphenamin must be between 18 and 20 per cent.

5. Each lot must be tested for its arsenic content and toxicity.

6. For toxicity tests, at least four or five albino rats are to be used, non-pregnant, weighing from 100 to 150 gm. A 2 per cent. solution of neutralized arsphenamin in doses not less than 80 mg. per kg. body weight is injected. It is required that 60 per cent. of the animals injected survive at least forty eight hours. Animals are not to be anesthetized for injection and if more than one rat dies, tests are to be repeated. Special rules are given for feeding and caring for the animals used. Tests are also made, on samples submitted, by the U. S. Public Health Service. The Federal Trade Commission can withdraw from the market any lot designated. Detailed records of the tests for each lot are to be kept and furnished to the Federal Trade Commission.

The maximum tolerated dose of neo-arsphenamin must be not below 90 mg. per kg. body weight, with injections of a 2 per cent. aqueous solution, intravenously, at the rate of 0.5 c.c. per minute.

Such restrictions have done a great deal to make the products on the market safe for use and have undoubtedly reduced the number of unfavorable reactions following injection.

Elbert Clark, Chicago.

UEBER DAS SKLEROEDEM UND SEINE BEZIEHUNG ZUR SKLERODERMIE (THE RELATION OF SCLĚREDEMA TO SCLERODERMA). A. Buschke, Dermat. Wchnschr. **70**:17 (Jan.) 1920.

Buschke gives further observations of the case which he described in 1902 as scleredema (Sklerödem) and also a summary of reports of cases of the same disease which have since been published. He sums up in part the characteristics of the disease thus: "A hardening (Versteifung) of the deeper layers of the cutis, the subcutaneous tissue, and most likely, to some degree the fascia and musculature. The disease apparently begins acutely, in most cases, on the neck spreading on to the face, the upper arms and the trunk to the abdomen. The lower extremities may be involved but seldom are. At the beginning the patients may be affected with weakness and prostration or may feel perfectly well. It has most frequently followed influenza-like affections, scarlet fever and parotitis but it cannot be denied that the former may have been a part of the disease itself. There is no pain, only a feeling of tenseness and rigidity. The movements of the body and breathing may be more or less interfered with by the latter. The skin usually looks pale or infrequently may be slightly cyanosed ,and the upper layers have a velvet-like feel. The induration lies in the deeper parts, has a cartilaginous feel and does not pit on pressure. . . . No disturbances of cutaneous sensations or sweat secretion worth mentioning are present. The full development of the disease may take place rather acutely in weeks or it may take months. It may last months or years but either regresses slowly to complete recovery or apparently some of the induration may remain indefinitely. . . . Histologically the disease shows no inflammatory reaction but is a deposit of a homogenous exudate which presses apart the connective tissue without involving the elastic tissue, the upper layer of the cutis, or the epidermis. There is no atrophy or disturbance of pigmentation. Nothing is definitely known as to the nature of the exudate but Noble has shown that it is not a simple edematous fluid but a deposit of a solid (festen) substance."

Since the genesis of the disease is not clear, the author goes on further to compare it with other similar affections. It differs from diffuse scleroderma in that it has a better prognosis, does not end in atrophy and pigment loss and does not affect the superficial layers of the cutis and epidermis. The author believes that some of the cases of diffuse scleroderma which have had a benign course, healing without permanent changes, are not examples of this disease at all but are scleredema and he cites certain examples from the literature. "Especially in the French literature is the description of acute scleroderma and its course so strikingly like Sklerödem, which Noble has called attention to, that by closer inspection many cases would undoubtedly be found which belong to our disease and should be separated from scleroderma."

Buschke also differentiates it from Fettsklerem (sclerema neonatorum) and from the scleredema of infants (edema neonatorum). He sees, however, a decided likeness between scleredema of adults and the so-called scleroderma of infants, of which only eleven cases have been described, and believes that a portion of the latter at least are examples of scleredema.

Ketron, Baltimore.

TRAITEMENT DE LA SYPHILIS NERVEUSE PAR LES INJECTIONS NOVARSENICALES A PETITES DOSES REPETEES ET PROLONGEES (THE TREATMENT OF NERVOUS SYPHILIS BY REPEATED AND SMALL DOSES OF NEOARSPHENAMIN). J. A. Sicard, Presse méd. (May 8) 1920.

Sicard claims to have obtained noteworthy results in the treatment of tabes, paresis, syphilitic paraplegia and hemiplegia by the daily administration of neo-arsphenamin subcutaneously or intravenously in doses not exceeding 0.15 gm. over an extended period. He has given as much as 50 gm. within a space of two years. He believes this method of treatment to be less dangerous than weekly injections of larger doses and superior in its results in nervous syphilis and in its effect on the Wassermann test in the blood and spinal fluid. He has not observed any nitritoid reactions. Toxic reactions fall chiefly within three groups:

(1) Dermatitis: Following the injection of from 0.5 to 3 gm. of neo-arsphenamin an erythema occurs in from 6 to 8 per cent. of the cases. It is not of serious significance, and treatment need be interrupted for a few days only. A dermatitis may occur later in the course of injections (5 to 10 gm.) and is of grave significance. It may result in alopecia, keratosis of the palmar and plantar surfaces, ulceration of the skin and mucous membranes, purpura, hemorrhages from the tongue, tonsils and pharynx. Sicard believes that certain lots of arsphenamin are more apt to produce this serious reaction.

(2) Loss of Ankle Jerk: In about 60 per cent. of cases following the administration of from 7 to 10 gm. of neo-arsphenamin there is a progressive diminution of the ankle jerks leading to its complete and permanent abolition. There is no muscular weakness or sensory changes with the exception of formication in the toes and soles in occasional cases. In only one case was the patellar reflex abolished. These changes exert a favorable influence in spastic paraplegia.

(3) Icterus: This occurs in about 2 per cent. of cases and is benign, disappearing in from three to four weeks.

Zimmermann, Baltimore.

ECZEMATOID EPIDERMOPHYTON INFECTION IN CHINA. H. Dold, China M. J. **33**:133 (March) 1919.

Dold found many cases of inflammation of the feet of the type he calls eczematoid inflammation of a vesiculopustular, dysidrotic type. He found this condition common among the Chinese, but seldom found it among white foreigners living in China. His cases are similar to those in European countries and in America, except that in his cases the process spreads to the plantar and dorsal regions and finally covers the whole or almost the whole surface of the foot. He classifies his cases into four main types: (1) the vesicular type, a sudden appearance of a sago grain-like vesicular eczema accompanied by intense itching; (2) chronic intertriginous type, desquamation of the skin in the peripheral zones and formation of whitened sodden masses of epithelium between the toes; (3) chronic hyperkeratotic type, formation of masses of overgrown horny layers, especially on the plantar surface; (4) pyodermic type, due to secondary infections.

The disease is more common in the southern part of China and more frequent during the summer. The condition heals or at least diminishes during the winter months and recurs in the summer. Some cases persist throughout the year.

In ninety-four of ninety-eight cases the disease occurred only on the feet; in two cases only on the hands; in two cases only in the genitocrural region; in one case on the feet and one hand, and in another case both feet and the right axillary region were simultaneously affected.

Microscopic examinations were done in all of the ninety-eight cases and in ninety-five the fungi could be demonstrated. Repeated examinations of the lesions should be made in those proving negative on the first examination.

Culture in Sabouraud's medium was tried in thirty-one cases and in only fourteen cases was the attempt successful. Dold considers the fungus identical with the one of Sabouraud's *Epidermophyton inguinale*.

He thinks that the disease in question is caused by *Epidermophyton inguinale* (Sabouraud) and the condition described by Martin Costa in Brazil, by Castellani in Ceylon (dermatitis rimosa of the toes) and by Cantlie in Hongkong ("Foot-tetter," "Dermatitis bullosa plantaris") are manifestations of infections with the same or closely related fungi.

Experimental transmission has been produced by him on two occasions from a pure culture of the organism.

Gutierrez, Manila.

LE CANCER DE LA DERMATOSE PRECANCEREUSE DE BOWEN (THE CANCER OF THE PRECANCEROUS DERMATOSES OF BOWEN). J. Darier, Ann. de dermat. et syph. **1**:49, 1920.

Darier is impressed with the fact that aside from the primary cancers of the skin, such as the spinocellular epithelioma, basal cell epithelioma and novocarcinoma, we meet types of cutaneous epithelioma which differ from the above in clinical evolution and histologic structure. In this group should be included the cancer developing in the precancerous dermatosis of Bowen, and Darier feels that the latter condition will be found frequently as it becomes better recognized. Darier describes a case in which almost the entire face was involved by a vegetating dermatosis with carcinomatous change. Diagnosis was difficult, and vegetating tertiary syphilis, tuberculosis, pemphigus vegetans, some mycotic disease and an unusual type of epithelioma had to be considered. The latter diagnosis was finally established. The features which differ from spinocelled epithelioma were the absence of pearly margins, the relative softness and particularly the great superficial extension without deep adherence, while the rapid progress and early glandular involvement did not conform to the picture of basal cell epithelioma. As the patient died the author gives detailed necropsy and histologic findings. Darier concludes that the cancer of the precancerous dermatosis of Bowen has clinical and histologic characteristics so well defined that a diagnosis can be made even in the absence of history of the beginning and evolution of the condition.

Clinically, the distinguishing features are its superficial rather than deep extension, its vegetating rather than ulcerative tendency; the formation of circumscribed plaques of conglomerated excrescences, separated by deep furrows, covered with scaly crusts and stippled with white points resembling milium. Its extension is rapid; it can produce profuse hemorrhages; it is accompanied by adenopathy, the glands being small, multiple and discrete; the metastases are lymphatic and can give rise to visceral involvement. The histologic structure is still more characteristic, and is given in detail.

Radical and early treatment is advised, surgical measures being preferable.

Senear, Chicago.

FURTHER INVESTIGATIONS ON THE CHEMICAL NATURE OF MARGOSIC ACIDS (FATTY ACIDS OF THE NIM OR MARGOSA OIL). RECENT CONCLUSIONS DRAWN FROM EXPERIMENTAL AND CLINICAL USE OF MARGOSATES AND ETHYL ESTER MARGOSIC. K. K. Chatterjee, Indian M. Gaz. **54**: 171 (May) 1919.

After discussing the chemical properties of this drug, Chatterjee takes up the action of the ethyl esters margosic and margosates. Chatterjee thinks the antisyphilitic properties of margosates are due to their being soaps of a special kind as they contain a fatty acid of a peculiar chemical formula. Soap acts chiefly by a process of hydrolysis induced either by its coming in contact with water or by the enzymic activity of the fluid tissues of the body. Ethyl ester margosic has these two characteristics: 1. It is in loose chemical combination and therefore is more readily hydrolyzed than potassium margosate. 2. Its margosic content is higher than that of potassium margosate.

Chatterjee thinks it not unlikely that concurrently with the process of hydrolysis the lipoid-globulin or the protective substance of the serum is broken up and the organism of syphilis is set free. It is possible for the organism to be hydrolyzed but in clinical conditions this renders the organisms inert and only in some instances is the destruction complete. Hydrargyri margositas was therefore introduced, combined with the ester. The metallic mercury is liberated and becomes fixed to the hydroxyl groups and so alters the arrangement of its ions that the protoplasm is disintegrated and the parasite killed.

Chatterjee then discusses the action of the drug on syphilis, leprosy, skin disease, filariasis, septic infections and ulcers.

Of twenty-seven cases of syphilis treated with potassium margosate, ethyl ester margosic and ethyl ester margosichydrargyri margositas, the lesions disappeared most quickly by the treatment of ethyl ester margosichydrargyri margositas.

Cases of Leprosy: Tuberculous, maculo-anesthetic and mixed types have been treated. In three patients the treatment has been suspended; eight are still under treatment. In the first three cases treatment was commenced with potassium margosate. One of these gave up treatment after making satisfactory progress. The other two patients made steady progress with potassium margosate, but progress was more marked and rapid after ester treatment was commenced.

Patients with skin disease have been treated with satisfactory results. The following conditions have been treated: eczema, erythema iris, scleroderma (localized), tinea affections, pedicular conditions of the scalp and trunk, scabies, erythrasma, dermatitis (exfoliative and ulcerative) and diffuse psoriasis.

Gutierrez, Manila.

A CASE RESEMBLING YAWS. A. J. Noronha, Indian M. Gaz. **54:** 178 (May) 1919.

Following an injury from a broken bottle, a Hindu lad, aged 15 years, had an ulcer and granulations. One month or so after this accident he noticed a scattered eruption all over his body. On examination he was found to have round his anus and over the scrotum extensive condylomas and also scabies on the trunk, genitals and extremities. Raised condylomatous yellowish patches, the size of a split pea, were present on the forehead, lips, trunk and extremities. These were all uniform, differing only in size. The Wassermann reaction was + + + +.

Gutierrez, Manila.

LA SYPHILIS NEUROTROPE, EXISTE-T-ELLE (IS THERE NEUROTROPHIC SYPHILIS)? Maurice Page, Presse méd. **28:**447 (April) 1920.

According to Page, two distinct types of syphilis exist, the ordinary syphilis "dermatrope" which may give rise to tabes and general paralysis, but rarely and with special characteristics, and a special type of syphilis "neurotrope" having an affinity for the nervous system. The difference is due to a variation in the spirochete itself and not to a predisposition on the part of the affected tissues. He calls attention to the scarcity of skin, mucus and bone tissue involvement in the neurotropic type. The husband or wife of the diseased one often is not infected. The children of tabetic and paretic persons, although showing a certain psychic disharmony, are usually exempt from hereditary syphilis.

Because of the difficulty of impregnating the nerve cells with antisyphilitic treatment, the author has conceived the idea of adding to the treatment the action of a serum or a toxin. He gives three injections of animal tuberculin and follows this with six doses of novarsenobenzol or arqueritol (interval not given). Collin prefers the serum of Marmoreck or the serum of Roux can be given. The object of the preliminary injections of a serum or toxin is to produce a "cataclysme de l'organisme" destined to cause a discharge of opsonins and a leukocytosis as great as possible, so that the arsenic or mercury will have a better chance of reaching the nervous substance. The author admits that further time is necessary to prove the value of this method of procedure.

Ketron, Baltimore.

ANTE-NATAL AND POST-NATAL SYPHILIS. John Adams, Brit. M. J. **1**:603 (May 1) 1920.

At a meeting of the Hunterian Society, Adams demonstrated a number of cases that had been treated at the Venereal Disease Center for Pregnant Women.

In the two years 1917 and 1918, fifty-eight mothers were treated. Twenty-five of the babies gave a positive Wassermann reaction at birth, and twenty-seven gave a negative reaction. There were six still-born babies. Adams concludes that treatment of pregnant women could be carried up to the day of confinement with safety and success, and a mother so treated might give birth to a baby with a negative Wassermann.

The treatment of syphilitic infants began immediately after birth, and consisted of the combined injection of galyl in glucose, and gray oil. Children so treated became healthier, put on weight, and their blood became negative and remained so.

This method was used: A dose of 1.5 cg. is injected into one buttock on the day after birth, and repeated after one week. The dose is gradually increased up to 5 cg. Hydrargyrol with chalk is given by mouth and intramuscular injections of gray oil, beginning with ¼ grain and increasing up to ½ grain, are given every two weeks to the babies and to the mothers once a week.

Adams says that as a general rule, with this combined treatment the Wassermann test is negative about the seventy-eighth day.

Oliver, Chicago.

MEDICAL NEWS FROM KANSU. G. E. King, China M. J. **33**:38 (Jan.) 1919.

Kansu is immediately south of the Mongolian plateau, with a population of from 5,000,000 to 10,000,000. Incidence of disease is influenced in the central part by the presence of Tibetians, and in the northern by Mongolians.

Smallpox, occasional epidemics of diphtheria, measles, mumps and scarlet fever occur. Scarlet fever is regarded as a disease newly imported to China. Malaria is not present in the northern zone. Some parts of the province show much goiter, which the native regards as due to the drinking of spring water or the water of mountain streams.

Leprosy is rare in a greater part of the province, but on the Tibetian border, in the center of Toochon, Howchow and Sinay it is known and feared.

The most common form of carcinoma is epithelioma over the trochantor induced by irritation from sleeping on the hot K'ang. Of tropical diseases, there are cases which resemble kala-azar; elephantiasis of the lower limbs has been observed.

One disease that the author wished diagnosed is what he calls progressive congenital angioma. The patient was 25 years old. A nodule the size of a bean, hard and of dark blue color was first noticed on the scapula. It grew slowly and painlessly till it attained the size of a pear. Other lesions appeared and the disease progressed in exacerbations annually in the spring and autumn. Intense varicosity of the vessels of the left arm and scapular region are now present. The bones and muscles are atrophied.

Gutierrez, Manila.

INFECTIONS AND VACCINES. Paul G. Wooley, J. Lab. & Clin. Med. **5**:543 (May) 1920.

"Vaccination has for its aims: (1) The initial increase of resistance of the host so that invasion by bacteria is made more dfficult or, in the extreme case (smallpox), impossible. (2) To so modify the fluids of the body that once an organism has invaded the body it is not able to survive the condition which discourages parasitism (typhoid). (3) To so modify the fluids that in the case of developed parasitism, the bacteria are eventually killed (furunculosis). It is this latter instance in which we are especially interested at this time."

Autogenous vaccines are to be preferred to stock vaccines. The value of mixed vaccines, even though autogenous, is questionable and their use unscientific. It were more advisable to use a known unmixed stock vaccine, a carefully studied polyvalent vaccine, or a single purified protein.

"Finally, and as practically as possible, vaccines (autogenous) seem to be useful in the following infectious disorders:

"(1) Furunculosis and localized abscesses in soft tissues; (2) acne vulgaris: (3) colon bacillus, pyelitis and cystitis; (4) chronic gonorrhea and gonorrheal rheumatism; (5) chronic bronchitis; (6) bronchial asthma of bacterial origin.

"Vaccines seem to be of little or no value in (1) infection of bone or infections in cavities with rigid walls; (2) infection of the intestinal tract: (3) infection of the uterus and adnexa.

"Vaccines are contraindicated in (1) acute infections and infectious diseases; (2) septicemia and pyemia in the acute stages; (3) malignant endocarditis."

Elbert Clark, Chicago.

THE VALUE OF LUETIN IN AN OUTPATIENT DEPARTMENT.

Alfred E. Meyers, Arch. Pediat. **37**:223, 1920.

The writer in an interesting article, records his experience with injections of luetin in the Outpatient Pediatric Department of the University of California Medical School. Feeling that every case of hereditary syphilis, whether active or latent, would show some stigmas of abnormal development, Wassermann and luetin tests were made on every child who did not score 100 from a developmental standpoint. The reason for their coming to the clinic, as well as the suspicious points in their history or physical examination, were noted. One hundred and sixty-eight cases were tested; 61 per cent. were males, 39 per cent. females. The oldest child was 18 years, the youngest 7 weeks. The Wassermann and luetin tests were both positive in 17.8 per cent.; the Wassermann negative and the luetin positive in 47.6 per cent.; both were negative in 28.5 per cent. The total number of positive reactions was 65.4 per cent., and in practically every case that gave a positive luetin reaction, there was something in the physical findings or the history indicative of syphilis. The majority of reactions were of the papular type; after forty-eight hours there appeared at the site of injection a definitely indurated papule, from 5 to 12 mm. in diameter, surrounded by a zone of redness.

The author's conclusions are:

1. The luetin test is more reliable in congenital syphilis than the Wassermann test.

2. At least 65 per cent. of congenital syphilitic patients will react positively to the test.
3. It causes no constitutional reaction.
4. It is more important to do a routine luetin test in the clinic than the von Pirquet test, providing the material can be obtained.

Oliver, Chicago.

CONTRIBUTION A L'ETUDE DE LA PATHOGENIE DU SOL-DISANT SYPHILOME ANO-RECTAL, FOURNIER (CONTRIBUTION TO THE STUDY OF THE PATHOGENICITY OF THE SO-CALLED ANORECTAL SYPHILOMA OF FOURNIER). O. Jersild, Ann. de dermat. et de syph. **1**:62, 1920.

Jersild carefully reviews the question of the anorectal syphiloma of Fournier, gives the detailed findings in six cases observed by himself, and concludes:

1. All findings show that patients with characteristic lesions of this type are syphilitic.
2. The fixed localization of the rectal infiltration indicates an affection anatomically determined.
3. The pathogenic mechanism is as follows: (*a*) Some lesions (chancre, chancroid, etc.) of the anoperineal region, with inguinal lymphadenitis, arrest of the lymphatic circulation in the inguinal glands or in the afferent lymph vessels of the glands. (*b*) Turning of the lymph of the anogenital region by the rectal lymphatics toward the glands of the mesorectum. (*c*) Anorectal adenitis (obliteration posteriorly). (*d*) Lymphatic stasis between the two obliterations mentioned in (*a*) and (*c*).

Senear, Chicago.

ZUR DIAGNOSE UND THERAPIE DES BENIGNEN MILIARLUPOIDS (BOECK) (THE DIAGNOSIS AND TREATMENT OF THE BENIGN MILIARLUPOIDS [BOECK]). Gertrude V. Bombard, Dermat. Wchnschr. **70**:161 (March) 1920.

The author describes a case showing the three forms—small nodular, large nodular and diffuse infiltrating—of miliarlupoid. The patient was a woman, aged 33, and the eruption was limited to the face and upper extremities. There was glandular enlargement and chronic nephritis and roentgen-ray examination revealed a small infiltration in the lungs and changes in the bone and periosteum of the left upper arm. The Sachs-Georgi reaction was positive. Wassermann and Pirquet reactions were negative. Animal inoculation with material obtained at biopsy gave negative results. The author believes from her observations of this case that benign miliarlupoid is clinically and histologically a well defined, bacillary, general disease which is most likely a special, mild form of tuberculosis.

The case was treated with intravenous injections of "Silbersalvarsan" but without improvement. Krysolgan (a gold preparation prepared by A. Feldt) was then tried and after several injections the skin lesions as well as the periosteal thickening disappeared, leaving only the telangiectasia. The lung condition, however, showed no improvement and was perhaps worse.

Ketron, Baltimore.

EINE TUBERCULINREACTION DER LYMPHGEFAESSE (A TUBERCULIN REACTION OF THE LYMPH VESSELS). Engwer, Dermat. Wchnschr. **70**:188 (March) 1920.

The author describes a case of tuberculosis verrucosa cutis on the hand in which there had been transplantations by way of the lymphatics up the arm. A tuberculin test on the affected arm had caused an acute inflammatory reaction in the affected lymph vessels.

Ketron, Baltimore.

SOME SURGICAL ASPECTS OF SYPHILIS. W. P. Coues, Boston M. & S. J. **182**:582 (June 3) 1920.

The author emphasizes the worthlessness of a negative report on a routine Wassermann test and the value of skeletal radiography as a help in latent syphilis. He calls attention to certain conditions in which syphilis is masquerading as a surgical condition complicating a surgical case:

1. Cervical adenitis due to tertiary syphilis is mistaken for tuberculous adenitis and Hodgkin's disease.

2. Deep seated syphilitic mediastinitis is sometimes mistaken for hopeless malignant disease.

3. Obscure conditions simulating ordinary bursitis or synovitis are quickly cured symptomatically when a proper diagnosis is made.

4. Syphilitic bone disease at times underlies varicose veins of the legs and varicose ulcers. Not infrequently specific ulcers of the leg are diagnosed as varicose because the patient has varicose veins.

5. In nonunion and delayed union of fractures, and repeated fractures from slight trauma, the possibility of syphilis must always be borne in mind. The author mentions one clinic in which every case of ununited fracture for a year gave a positive Wassermann reaction.

6. Gummatous infiltration of the testicle is not infrequently operated on for sarcoma, teratoma or tuberculosis, and is often confused with an enlargement due to the gonococcus.

7. Tabetic arthropathies, with or without ulceration, are not infrequently incorrectly diagnosed, especially ulcer on the sole of the foot.

8. Five or six per cent., or possibly more, of ulcers of the stomach are now said to be syphilitic.

Lane, Boston.

ZUR FRAGE DER GIFTFESTIGKEIT DER SPIROCHAETEN (RESISTANCE OF SPIROCHETES TO DRUGS). Gustav Fantl, Dermat. Wchnschr. **70**: (Feb.) 1920.

Stejskal (*Dermat. Wchnschr.,* 1919, No. 41) had shown that arsphenamin caused spirochetes to disappear less rapidly from lesions of patients who had previously received mercury than from those of untreated cases and concluded that the organisms developed a resistance to arsphenamin as a result of the mercurial treatment. Fantl's experiments supported this conclusion. Spirochetes derived from mercury-treated patients (mercuric chlorid and salicylate intramuscularly) remained motile in dark field preparations for a longer period than from untreated cases. In the untreated cases the average duration of motility was fourteen hours in contrast to twenty hours in the treated. Resistance was also tested by the effect of adding arsphenamin (0.01 per cent.)

and mercuric chlorid (0.2 per cent.) to serum in dark field preparations. The spirochetes from untreated cases lost their motility within a short time, while those from treated cases remained motile for hours. The data from only a few cases are given in detail.

Zimmermann, Baltimore.

ORIENTAL SORE OR BAGDAD BOIL. D. J. Harries, Indian M. Gaz. **54**:325 (Sept.) 1919.

Harries discusses the modes of transmission and relationship between kala-azar and oriental sore, saying that the organisms found in the sore are indistinguishable from those found in kala-azar. He further points out that patients suffering from kala-azar do not suffer from oriental sore, and thinks that the patient is rendered immune from the presence of one or the other.

After discussing the various symptoms and phases of the disease, he outlines a course of treatment as follows:

Internal: The best results have been obtained by intravenous administration of a 1 per cent. solution of antimony tartrate, starting with 5 c.c. and gradually increasing the amount to 10 or 15 c.c. It may be given daily or every other day.

Local Measures: (1) Local application of antiseptic solutions, (2) ionization, and (3) complete excision. Complete excision has given the best results. When the sores are localized it is the method of election, but when they are multiple other methods should be resorted to.

Gutierrez, Manila.

UEBER DER HISTOPATHOLOGIE DER DRUSENERVEICHUNG IN FRUHSTADIUM DER LUES (THE HISTOPATHOLOGY OF GLAND SOFTENING IN EARLY SYPHILIS). A. Finsterlin, Dermat. Wchnschr. **70**:97 (Feb.) 1920.

Finsterlin examined the inguinal glands of a patient with multiple chancres in which softening of the glands could be explained only on the basis of syphilis. The fluid from the fluctuating glands was negative on bacteriologic examination. He emphasizes the following changes: mesarteritis, new capillary formation, plasma cell infiltration and areas of necrosis in the central portion of the glands. He attributes the necrosis to pressure on the vessels by the dense infiltration, a process analogous to that in chancres and in the bubonuli occurring along the dorsal lymph vessels of the penis. Individual resistance must also be taken into consideration.

Zimmermann, Baltimore.

TREATMENT OF PRURITUS ANI BY X-RAY RADIATION. William J. Young, Am. J. Roentgenol. **7**:116, 1920.

Young relates briefly his experience in treating pruritus ani with roentgen ray. The results for the most part have been commendable. Unfiltered doses of roentgen ray were used.

In the treatment of pruritus ani during the last four years he has depended entirely on fractional doses of roentgen ray given at weekly intervals, the dosage being governed by the infiltration of the anal tissues, from four to ten radiations constituting the treatment. In the cases treated, the results have varied from temporary improvement to seeming cure. His best results have been secured when working in conjunction with the proctologist, his part consisting of relieving the pruritus while the proctologist tried to correct the particular condition that operated as a causative factor.

His experience has been that recurrence of the pruritus depends on the amount of rectal pathology present.

Elbert Clark, Chicago.

THE DEEPER STRUCTURAL CHANGES ARISING FROM VARICOSE ULCERATION. Dudley H. Morris, Surg., Gynec. & Obstet. **30**:72 (Jan.) 1920.

It is unusual for a periostitis or osteomyelitis to localize beneath an ulcer. Instead, far reaching changes such as a diffuse periostitis or osteomyelitis of the tibia, fibula or both these bones develops, which is so diffuse as to extend throughout the entire shafts and involve even the epiphysis, and so chronic as to pass unnoticed by the patient. The inflammatory process apparently never reaches the stage of abscess formation, and if suppuration exists its products are absorbed into the system. Widespread vascular changes accompany this. The deep vessels, posterior tibial and peroneal show marked calcification which extends to the popliteal or above, and which occurs independently of the ulcer, but is most marked in those cases in which ulceration has been present for a long time.

The mechanism of the bacterial distribution to the parts of the bone remote to the ulcer is by way of the arterial wall and adjacent lymphatics.

Photographs of cases and of roentgenograms of the leg bones accompany this excellent and significant article.

Goodman, New York.

ON THE HISTOLOGICAL RESEMBLANCES OF ORIENTAL SORE TO EPITHELIOMA. William Macadam, Brit. J. Surg. **7**:28, 1919.

Macadam states that in examining a number of excised skin lesions of the type of Oriental sore he found that most of them showed the character of a chronic ulcer, but in two of them the histologic picture was practically indistinguishable from a squamous-celled carcinoma.

The first specimen of the latter two was taken from an ulcer of three months' duration in which typical *Leishmania tropicum* bodies were found. The accompanying drawing shows a picture closely resembling epithelioma, but with considerable round cell infiltration. The other specimen presenting a similar histologic picture, was taken from an ulcer on the lip.

Macadam notes that there is a possibility that some of these ulcers in their chronicity may take on the characters of true carcinoma, but he found no clinical evidence of such a change in the two cases cited. He also calls attention to the fact that in sores of some duration, in which early malignancy may be a probability, it may be impossible to detect the *Leishmania tropicum*, since the parasites tend to disappear in lesions of some months' standing.

Senear, Chicago.

AUTOPLASTIC SURGICAL TREATMENT OF BALDNESS. R. Passot, Presse méd. **28**:222 (April 17) 1920.

Passot reports a method of treating baldness by plastic operation. He takes pedunculated flaps from the hairy part of the scalp and moves them over to the bald areas. He reports successful results in six cases so treated.

TREATMENT OF SYPHILIS BY ANTISYPHILITIC SERUM OF QUERY. J. Dobriansky and T. Thompson, Lancet, **1**: 903 (April 24) 1920.

Dobriansky and Thompson give a brief report on this interesting subject. Query serum is prepared by inoculating monkeys with filtered cultures of *Spirochaeta pallida* on bouillon. When the monkeys so infected give a strong positive Wassermann reaction, they are bled and the serum is preserved in ampules. Dobriansky and Thompson report three cases of syphilis treated with this serum with great improvement. They are said to have been cases in which established methods of treatment had failed to relieve symptoms. One was a case of gummatous ulcers of the leg; the second a case of tabes with ataxic symptoms, and the third a tabes with lightning pains.

AN UNUSUAL CASE OF KELOID. Rutherford Morison, Brit. J. Surg. **7**:28, 1919.

Morison reports a case of keloid occurring in a negro, the lesion developing on the ears at the site of openings made for ear rings. In the photographs each of the tumors appears as large as the patient's head. Morison recalls that keloids are associated in some way with sepsis and chronic tuberculosis, and that on the skin burn scars and scars resulting from tuberculosis are their favorite sites. He believes that it is not generally recognized that similar growths are to be found elsewhere in the body, and he cites a number of such instances in lesions of the mouth and the gastrointestinal tract.

Senear, Chicago.

A CASE OF GENERALIZED ALOPECIA OF NERVOUS ORIGIN. Carlo Todde, Riforma med. **36**:382, 1920.

The author presents the case of a lieutenant in the Italian army, a man of 34, who after severe nervous shock caused by continuous bombardment during seven days, noticed the rapid falling out of his hair, accompanied by slight pruritus. The alopecia began on the head and soon spread to the eyebrows, beard and the rest of the body. In a few days the baldness was complete and generalized. The patient denied syphilis. The Wassermann test was negative. The observer could rule out ringworm, infectious diseases and other diseases that may produce alopecia. He thinks this case the result of intense nervous strain and violent emotions, which, perhaps, led to disturbances of the internal secretions, affecting the nutrition of the hair. Accordingly the author treated the patient with extracts of endocrinous glands. The final therapeutic results are not reported.

V. Pardo-Castello, Havana.

DIE SYSTEMATISCHE KOMBINIERTE STRAHLENBEHANDLUNG DER HAUTTUBERKULOSE, INBESONDERE DES LUPUS (THE SYSTEMATIC COMBINED RADIATION OF SKIN TUBERCULOSIS, ESPECIALLY LUPUS). G. A. Rost, Dermat. Wchnschr. **70**: 129 (Feb.) 1920.

The method described by the author consists of the combined use of the roentgen ray, ultraviolet light (Kromayer lamp) and artificial sunlight. The affected area was given a full roentgen-ray dose about every six weeks with a 1 to 4 mm. aluminum filter. The ultraviolet light treatments, with blue glass filter, were given between the roentgen-ray treatments at somewhat more frequent intervals. The reaction was allowed to disappear entirely before a roentgen-ray treatment was given. Besides this local treatment, the patients had general applications of artificial light (Künstlicher Höhensonne). These light baths exerted a good effect on the local disease, but the method by which this was accomplished is not known; an increase of the protective substances in the skin is a possibility. The author believes that pigmentation is not to be desired since it decreases the absorption of the light rays. The treatments were given about twice weekly, producing an erythema but no vesiculation. The time of treatment was prolonged as pigmentation increased but no treatments over thirty minutes long were given. When the pigmentation became great a depigmentation pause of several weeks was allowed.

KETRON, Baltimore.

SEPTIC FEVER OR SYPHILITIC SEPTICEMIA. D. McCoy, Indian M. Gaz. **54**:260 (July) 1919.

McCoy reports three cases in which the cause of the fever could not be determined. It was septic in character, not influenced by quinin. There was history of syphilis in all three cases, though gonorrhea was admitted by the patient in Case 1. The same patient had had several attacks of fever of the same character as the present while in German East Africa. There were no signs of syphilis in the three patients.

In these patients the fever subsided immediately after the administration of antisyphilitic remedies. The Wassermann reaction was positive in all three.

GUTIERREZ, Manila.

ENQUETE SUR LA FREQUENCE DES TUMEURS MALIGNES DE LA PEAU CHEZ LES INDIGENES NORD-AFRICAINS (FREQUENCY OF MALIGNANT NEOPLASMS OF THE SKIN AMONG THE NATIONS OF NORTHERN AFRICA). J. MONTPELLIER and H. MARCHAND, Bull. Soc. franç. dermat. et syph. No. 8, 317, 1919.

Montpellier and Marchand offer the observations of J. Brault in contradiction to the established idea that malignant neoplasms of the skin are rare or almost nonexistant among the natives of North Africa, and state that efforts are being made to collect statistics of the frequency of various types of malignant neoplasms of the skin as they occur in this region.

SENEAR, Chicago.

ARSPHENAMIN REACTIONS. JOHN F. MARTIN, J. A. M. A. **74**:18 (May 1) 1920.

The sequelae arising from arsphenamin medication may be thus classified: the incidents, slight untoward symptoms occurring in patients with normal tolerance to arsphenamin, such as vertigo, palpitation, disturbance of taste and smell, or slight nausea; the reactions, usually occurring in syndromes, and causing discomfort and sometimes incapacity, which may be ascribed to allergic or acquired susceptibility to arsphenamin, functional or organic complications, or toxic arsphenamin solutions; the grave reactions (sometimes fatalities), such as dermatitis exfoliativa, toxic jaundice, hemorrhagic encephalitis and gangrene; the accidents, such as thrombosis, phlebitis, and infiltrations about a vein.

LEVIN, New York.

TOKELAU (T. IMBRICATA). H. Jouveau-Dubreuil, China M. J. **33:** 223 (May) 1919.

Joveau, contrary to general conceptions that this disease is confined to warm countries and near the sea, found several cases of it in Szechwan which is far inland and where the climate is continental and temperate. He gives a good description of the disease and his method of treatment. This in brief consists in the application of a 10 per cent. ointment of chrisophanic acid to the legs and if the patient does not show any signs of poisoning the medicine is applied to the trunk and to the neck. He even treats the face with the drug, taking care not to get the ointment into the eyes.

Gutierrez, Manila.

CAUSES DU SYNDROME MALIN DANS LA SYPHILIS (CAUSES OF MALIGNANT SYPHILIS). G. Lacapere, Bull. Soc. franç. dermat. et syph. No. 8, 320, 1919.

As a result of observations made among the Arabs, Lacapere feels that malignant syphilids are the result of vascular hypotension, the latter usually being due to malaria in the cases studied. Among the better classes tuberculosis, anemia, etc., may produce this hypotension. He does not believe in the invocation of a malignant strain of spirochetes to explain these cases.

Senear, Chicago.

UEBER AORTENVERAENDERUNGEN BEI LATENTER LUES (CHANGES IN THE AORTA IN LATENT SYPHILIS). Erwin Pulay, Dermat. Wchnschr. **70:**177 (March) 1920.

Examination of latent syphilitics in a dermatologic clinic revealed eighty-five patients with aortic changes, forty-six men and thirty-nine women. The interval between infection and discovery of signs of aortitis varied from one to fifty years. Pulay advocates repeated examination of every syphilitic for signs of aortitis so that early and thorough treatment may be instituted. Roentgenology is most important and in many cases will be the only means of detecting the aortitis.

Zimmermann, Baltimore.

OBSERVATIONS ON THE COLLOIDAL GOLD REACTION WITH CEREBROSPINAL FLUID. Ellis Kellert, Am. J. Med. Sc. **159:**257 (Feb.) 1920.

Attention is called to the fact that this reaction may at times be false and misleading and a number of cases are cited to illustrate the point. In seventy-five cases with negative reactions, 7 per cent. were false; 70 per cent. of positive syphilitic reactions had positive Wassermann reactions, while 6 per cent. had a positive gold curve and a negative Wassermann reaction. In tuberculosis 88 per cent. of reactions were correct, in acute meningitis 80 per cent. being most valuable in determining a cerebrospinal syphilis. Other diagnostic means should also be used to confirm these findings before treatment is begun.

It was found that spinal fluid contaminated with blood even in very small quantities could give a syphilitic curve and that positive results should be supported by other positive findings to be of value. The writer concludes by stating that he considers the Wassermann reaction and cell count in the spinal fluid to be of greater value than the colloidal gold curve.

Jamieson, Detroit.

RADIUM IN KELOID AND CAULIFLOWER GROWTHS ON SAME FOLLOWING EXTENSIVE BURNS. Harry B. Kurtz, Urol & Cutan. Rev. **24**:4 (April) 1920.

The writer reports the occurrence of deforming keloids in a man who had been burnt by hot lead. During the course of four months 5,000 mg. hours of radium was applied with ultimate cosmetic improvement.

Levin, New York.

BEITRAGE ZUR DIFFERENTIALDIAGNOSE ZWISCHEN PSORIASIS UNIVERSALIS UND DEN EXFOLIATIVEN ERYTHRODERMIEN (THE DIFFERENTIAL DIAGNOSIS BETWEEN GENERALIZED PSORIASIS AND EXFOLIATIVE ERYTHRODERMIAS). H. W. Siemens and Julius Thieme, Dermat. Wchnschr. **70**:9 (Jan.) 1920.

The author describes at length a case of universal psoriasis and takes up briefly the differential diagnostic points.

Ketron, Baltimore.

THE ETIOLOGY OF THRUSH. A. Castellani, J. Trop. M. **23**:17 (Jan. 15) 1920.

The author believes thrush is not such a simple condition as has been thought, but is due to a variety of fungi and not to the one variety of *Monilia albicans* (Robin) He recognizes two types of lesions—the white or gray-white and the yellow or yellow-brown, the latter being of rare occurrence.

Jamieson, Detroit.

GROUPED COMEDONES IN AN ADULT. E. G. Graham Little, Proc. Roy. Soc. Med. **13**:39 (March) 1920.

An eruption closely simulating acne vulgaris developed on the chest following the local application of camphorated oil.

Guy, Pittsburgh.

CASE OF CORNUA CUTANEA OF THE FEET. A. M. H. Gray, Proc. Roy. Soc. Med. **13**:57 (March) 1920.

A case of cutaneous horns developing on the side of "corns" is discussed.

Guy, Pittsburgh.

NERVE DEAFNESS DUE TO CONGENITAL SYPHILIS. M. B. Kay, J. A. M. A. **74**:1162 (April 24) 1920.

Kay reports three cases in which syphilis produced deafness in all three children of one family in the same manner, every other part of the body escaping but the eighth nerve. Owing to the fact that at least a year had elapsed before signs of deafness developed, Kay believes that these were undoubtedly cases of "late hereditary syphilis." Each of the children was put on increasing doses of potassium iodid, reaching 35 grains, three times a day. The general result has been good.

Waugh, Chicago.

CASE OF LICHEN PLANUS AND PSEUDOPELADE. S. E. Dore, Proc. Roy. Soc. Med. **13**:13 (Dec.) 1919.

A woman, aged 28, presented lesions of lichen planus and pseudopelade. In discussing the case Dr. Whitefield expressed the opinion that more than one disease is included under pseudopelade or cicatricial alopecia. One condition, in which there is scarring with alopecia, he considers a scleroderma. The other condition, in which there is no scarring or obvious atrophy, he considers a probable infective process and suggests strong antiseptics and a guarded prognosis.

Guy, Pittsburgh.

CONTRIBUTION A LA TECHNIQUE DE LA REACTION DE WASSERMANN (CONTRIBUTION TO THE TECHNIC OF THE WASSERMANN TEST). M. Goubeau, Bull. Soc. franç. de dermat. et syph. **7**:265, 1919.

Goubeau presented before the Society Lagage's opinion of the Wassermann reaction and stated that the latter believes the principal cause of contradictory results in the test is faulty titration of complementary power of serum. Lagage also proposes: (1) a common antigen which has been carefully titrated; (2) abandoning the "drop" method of measuring, and (3) the use of colorless human serum from patients who have not eaten recently.

Senear, Chicago.

A SIMPLE METHOD OF CULTIVATING THE MICRO-ORGANISMS OF ACTINOMYCOSIS. M. H. Gordon, Brit. M. J. **1**:435 (March 27) 1920.

The actinomycosis fungus can be readily cultivated in ordinary nutrient broth to which a few drops of fresh human blood have been added. It is advisable to sow the material in two blood mixtures, one of which is covered by a layer of oil, 1 cm. deep. After incubation for a few days at 37 C. the actinomyces fungus can be seen growing at the foot of the tube in small white masses. As a rule, growth occurs first in the broth covered with oil, but when other bacteria are present the actinomyces may come up first in the aerobic tube.

Vaccines may be prepared and used successfully.

Goodman, New York.

SILVER SALVARSAN. H. Boas and A. Kissmeyer, Ugesk. f. Læger **82**: 196 (Feb. 5) 1920; Idem., A. Korsbjerg, p. 196.

Boas and Kissmeyer report good results in sixty-two cases of syphilis treated with silver arsphenamin. They think it is as effective as the old arsphenamin and more soluble. Korsbjerg writes on the same subject, reviewing the literature, and gives his judgment, based on thirty-two cases, which agrees with that of Boas and Kissmeyer.

CASE FOR DIAGNOSIS. E. G. GRAHAM LITTLE, Proc. Roy. Soc. Med. **13:** 13 (Dec.) 1919.

A school boy, aged 15, had a translucent waxy tumor on the inner surface of the right ala nasi, about one-fourth inch above the surface and one-half inch in diameter. It had recurred after attempted surgical removal, and radium treatment had not affected it. Diagnoses of rodent ulcer, milium (atypical) and sebaceous nevus were entertained.

GUY, Pittsburgh.

A METHOD OF TREATING TINEA. C. J. GLEASON **1**:219 (Feb. 14) 1920.

Gleason has used a thin layer of the chrysophanic acid ointment (30 grains to the ounce of lanolin), spread all over the dhobie or washerman's itch, and a little beyond the outer borders of the tinea. A roentgen-ray application is made (dose not definitely given), but measured according to the author's experience. After the treatment the ointment is wiped off the skin, and in 90 per cent of the cases treated in this way one application was sufficient to cure; in a few a second was given to make certain. Neither the ointment nor the roentgen ray alone gave such results.

GOODMAN, New York.

LES HEMATODERMITES D'ORIGINE SYPHILITIQUE INDIRECTE. (INDIRECT HEMATODERMATITIDES OF SYPHILITIC ORIGIN). DR. LEREDDE, Bull. Soc. franç. de dermat. et syph. **7**:282, 1919.

Leredde used antisyphilitic treatment in three cases, respectively, prurigo, acute eczema and an undiagnosed itching dermatitis. The father of the first patient had syphilis; in the second case both parents had syphilis; while in the third the patient gave a positive Wassermann reaction. Marked improvement in the skin condition followed antisyphilitic treatment, and Leredde suggests that many dermatoses are indirectly due to syphilitic infection.

SENEAR, Chicago.

A CASE OF HERPES ZOSTER. H. W. BARKER, Lancet **197**:1136 (Dec. 29) 1919.

The case reported is of unusual interest because two distinct areas on the same side of the body were involved: the ophthalmic division of the fifth nerve and the seventh intercostal nerve. The author was unable to find any record of zoster occurring simultaneously on the face and trunk.

WAUGH, Chicago.

A CASE OF MULTIPLE INFECTIVE LYMPHANGIO-ENDOTHELIOMATA. GEORGE PERNET, Proc. Roy. Soc. Med. **13**:17 (Dec.) 1919.

About eight years after the great toe had been amputated on account of a malignant growth, there appeared a number of small brownish, translucent appearing, cherry-stone-sized tumors over the shin of the same leg. The microscopic picture suggested endotheliomas to the pathologist. Dr. Adamson pronounced it the typical structure of carcinoma deposits in the lymphatics.

GUY, Pittsburgh.

SCLERODERMIE ET TRAUMATISME (SCLERODERMIA AND TRAUMATISM). R. Burnier, Bull. Soc. franç. de dermat. et syph. 7:294, 1919.

Burnier describes a case of scleroderma occurring at the site of a traumatism and limited to the injured area.

Senear, Chicago.

CASE FOR DIAGNOSIS. J. M. H. MacLeod, Proc. Roy. Soc. Med. **13**: 22 (Dec.) 1919.

The patient had a large number of lesions on the legs, feet, arms, back and shoulders. For the most part they comprised depressed scars, the result of breaking down nodules. Glanders, dermatitis artefacta, sporotrichosis and scrofulous gumma were considered in diagnosis.

Guy, Pittsburgh.

UN CAS DE GRANULOME ANNULARE (A CASE OF GRANULOMA ANNULARE). Milan, Saupher and Thibaut, Bull. Soc. franç. de dermat. et syph. **7**:269, 1919.

The authors describe the clinical, physical and microscopic findings in a case of granuloma annulare. Findings strongly suggestive of tuberculosis were present.

Senear, Chicago.

CASE OF "ERYTHRODERMIE CONGENITALE ICHTHYOSIFORME." H. W. Barber, Proc. Roy. Soc. Med. **13**:22 (Dec.) 1919.

The condition began at the age of 3, when the skin of the trunk and limbs gradually became roughened, in places reddened and covered with horny growths. In some places the skin was normal. A peculiar musty odor, such as Darier described in his case, was noted.

Guy, Pittsburgh.

TACHES ET TUMEURS PIGMENTEES DE LA PEAU CHEZ UN EPILEPTIQUE (MACULES AND PIGMENTED TUMORS OF THE SKIN IN AN EPILEPTIC). Olga Eliascheff, Bull. Soc. franç. dermat. et syph. No. 8, 324, 1919.

Eliascheff discusses a case in which the diagnosis rests between leprosy, xanthoma and Kaposi's sarcomatosis. Darier felt that the case was related to the latter disease but that it was a pigmentary, nonhemorrhagic form.

Senear, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, May 4, 1920

John E. Lane, M.D., *Chairman*

HEMIATROPHIA FACIALIS. Presented by Dr. Wise.

The patient was a little girl, aged 5, from Dr. Fordyce's clinic. The right side of her face was flattened. Two years previously she had been presented before the Section with a typical scleroderma, which was said to have followed the extraction of a right lower molar. She had been treated with pituitary and thyroid extract, and while the skin softened, the atrophy of the skin and superior maxillary bone on that side remained unaffected. There was no paralysis or sensory disturbance.

DISCUSSION

Dr. Levin told of a similar case presented by him at a previous meeting of the Section in which there was also atrophy of the bone. In this case the patches of scleroderma had disappeared under the administration of thyroid.

VON RECKLINGHAUSEN'S DISEASE. Presented by Dr. Trimble.

A child, about 12 years of age, presented an unusually early development of the disease. When the case was first seen it was thought to be only a pigmentation, but closer examination revealed tumors which were not at all pronounced.

DISCUSSION

Dr. Pollitzer said that in Recklinghausen's disease there was a triad of symptoms which this child presented—pigmentation, neurofibromas and mental deficiency. She was in a class in school in which her mates were 8 or 9. She was three or four years behind in her mental development.

TINEA UNGUIUM. Presented by Dr. Howard Fox.

P. A., a colored man, 25 years of age, under charge of the U. S. Public Health Service, had a disease of the nails which was first noticed nineteen months previously while he was serving as a soldier in France. He was working in a machine shop at the time and could not give any suggestion as to the origin of the condition. The right middle finger first became diseased, and within a month nearly all the fingers and toe nails had become involved. Since that time the process had progressed slowly, extending from the free borders of the nails toward their roots. Examination disclosed that all the nails of the hands were affected, except the little finger of the right and thumb and little finger of the left hand. All the toe-nails were likewise involved except that of the middle left toe. The nails showed varying degrees of dystrophy, affecting particularly the distal ends. One of the nails showed a slight chipping of the free border and a slight subungual hyperkeratosis—the patient stating that "all the nails began that way." There was an entire absence of paronychia, and no eruption was noted elsewhere. Three massive doses of roentgen ray given recently at monthly intervals had as yet caused no improvement. Several previous attempts to find the ringworm fungus had failed.

On the day after presentation a specimen which had remained for twenty-four hours in 40 per cent. sodium hydrate solution was examined and a mycelium and spores in great abundance were found. No growths had as yet appeared in a culture.

LUPUS VULGARIS. Presented by Dr. Gilmour.

The nose of F. L., a married woman, born in Italy, began to be red about eight years ago and progressed to the present condition. She was treated in the German Hospital about five years ago, and was under treatment there for about two years. She had had roentgen-ray treatment and also iodid injections, and about a year ago was treated with carbon dioxid in the DeMilt Dispensary.

INFECTIOUS ECZEMATOID DERMATITIS. Presented by Dr. Abramowitz.

Edward D., aged 10, of Italian parentage, was from the service of Dr. Fordyce at the Vanderbilt Clinic. The mother of the child stated that the skin condition had existed for two years. The lesions began in a small area on the right calf after an attack of pneumonia. The lesions on the neck and trunk were arranged in a band-like form about 2 inches wide and consisted of a thickened, erythematous small, papular, scaly dermatitis. The entire circumference of the leg was covered by a weeping and also purulent exudate, from which it was difficult to remove the bandages. An exposed cutis with numerous pustules and erythematous dermatitis completed the picture in this area. A few isolated crusted papules were present on the trunk. The inguinal glands were enlarged to the size of a bird's egg. The axillary glands were slightly enlarged.

DISCUSSION

Dr. Pollitzer said that the case impressed him as one of the most interesting of those presented. He wished to point out that the eczematous lesions presented a striking localization; they were limited to the extensor surfaces of the extremities, leaving the flexor surfaces entirely free—an unusual distribution for eczema. The case was one that could not be disposed of at a glance, but it seemed to him to be a prurigo eczematized by scratching.

Dr. Gilmour also inclined to the diagnosis of prurigo, and directed attention to the lesions in the groins. Had it been a virulent infection, some of these would doubtless have broken down. Such enlargements were common in prurigo.

Dr. Levin said that against its being an infectious eczematoid dermatitis was the presence of most of the lesions on the extensor rather than on the flexor surfaces, and the absence of any pustules or pustular patches. It seemed to be a case of chronic pruritus with a secondary eczema. A blood count should be made to rule out a blood condition.

Dr. Brenner (by invitation) said that he had been impressed by the idea that it was primarily a condition of general malnutrition and that probably in the zeal of the dermatologists more attention had been paid to local treatment than to a general study of the systemic condition. Recently a series of papers had been published on the suboxidation syndrome, which referred especially to the constituents of the blood; and by the elimination of fats and sugars from the diet and the substitution of cottonseed oil, etc., it had been possible to regulate the internal secretions so as to overcome the skin conditions. While the local condition need not be neglected, it would seem that more attention should be given to the general condition, i. e., a searching of the blood for creatinin and sugar, and the ascertaining of whether the lesions were not due to some internal condition rather than to a parasite. The same would apply to a great many dermatologic cases, as not enough blood work is done to ascertain what is happening to the nourishment of the skin, especially in children.

Dr. Pollitzer said he was in complete harmony with Dr. Brenner in not regarding all skin diseases as purely local processes. He thought Dr. Brenner was mistaken in attributing a contrary belief to dermatologists in general. While a large number of dermatoses were strictly disorders of the skin, there were a great many skin diseases in which the cutaneous disturbance was the result of an internal or systemic disease. This fact was so elementary that dermatologists did not think it necessary to refer to it in every case. The disease whose cutaneous manifestation we call prurigo is an excellent example of a skin disease produced as the result of a systemic disorder.

Dr. Brenner said that he had evidently been misunderstood, for he merely wished to emphasize the fact that one should remember that many skin diseases were due to systemic conditions and that one should guard against considering them purely local.

Dr. Levin said they had studied the blood chemistry of about 200 patients with cutaneous conditions. As a result of his experience, he believed the blood chemistry of this patient would reveal nothing abnormal, except possibly a low carbon dioxid content.

Dr. Bechet could not agree with the diagnosis of prurigo. He did not think that the presence of the enlarged glands necessarily indicated that the case was one of prurigo; they could be caused by septic absorption from an infectious eczema. The boy had a large scaly patch back of the ear which looked like a typical eczema. He was inclined to consider it a case of ordinary eczema with secondary infection and subsequent enlargement of the lymphatic glands.

Dr. Pollitzer remarked that while a great deal had been said about the eczematous lesions no one had referred to a different class of lesions which was noted particularly on the back of the patient and especially over the shoulder blades. This region was dotted with small discrete scratched papules and felt like a nutmeg grater. This was not eczema and did not harmonize with the diagnosis of eczema in other regions. On the other hand, a badly scratched prurigo could simulate an eczema. Those who dwelt mainly on the eczematous lesions should remember that there were other lesions that were distinctly those of prurigo. The distribution of the eczematoid areas, the occurrence of distinct lesions of prurigo, and the enlarged lymph nodes indicated prurigo. Whether or not the whole condition was due to leukemia or to some endocrine or other disturbance, would require further study.

Dr. Abramowitz said that the patient had come to the clinic the day before presentation, so that no detailed study had been made. The eruption to which Dr. Pollitzer referred was much more noticeable in the daylight. Most attention was attracted by the band-like eruption on the neck, arms, and trunk and the pyodermia of the legs, which might account for the enlarged inguinal glands. It was thought possible that the dry eczematous lesions elsewhere on the body had probably at other times also taken on the pyodermatous nature, and hence it was considered an eczematoid dermatitis. It was difficult to form any conclusion at present. The prurigo-like papules on the body would be watched to see whether they would develop into an eczema or disappear. No history of an exciting suppurative process could be obtained.

BLASTOMYCOSIS. Presented by Dr. Binford Throne.

A horse driver had a lesion about 3 by 4 inches in size and situated on the anterior surface of the left wrist. It was granulomatous in character, slightly verrucous, with miliary abscesses. The onset of the disease occurred in June, 1918.

The section showed blastomycoses.

TYLOSIS PALMARIS HEREDITARIA. Presented by Dr. Binford Throne.

Mrs. E. T., born in Italy, and her three children, aged 13, 11 and 4, respectively, presented themselves at Dr. Whitehouse's service at the Skin and Cancer Hospital, April 21, 1920. All showed extensive tylosis palmaris and the oldest, in addition to the palmar condition, had involvement of the plantar surface of both feet. In all cases the disease began early in infancy. Mrs. T. said that her mother showed the same condition. No history of consanguinity could be obtained.

PITYRIASIS ROSEA IN A NEGRO. Presented by Dr. Howard Fox and Dr. B. F. Ochs.

G. T., a negro, aged 38, presented on the trunk a fairly profuse eruption of superficial inflammatory scaly lesions of the punctate, macular and circinate type. The general eruption was of two weeks' duration, and several days before its appearance an unusual patch, oval in shape and an inch in length had appeared on the upper portion of the right thigh. The patient, who was a large robust man, apparently in excellent health, was unable to suggest any cause for the appearance of the eruption.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, May 25, 1920

George M. MacKee, M.D., *President*

NECROTIC GRANULOMA — TUBERCULOSIS? Presented by Dr. Winfield.

Miss H., aged 22, had been under observation since November, 1919. She was one of the bacteriologists of the Department of Health. In September, 1919, she was vaccinated; in a short time the vaccination became inflamed and purulent, but it finally healed after about six weeks, forming a keloid scar. While the inflammation in the vaccination was beginning to subside, a pustule developed on the arm about 2 inches from the vaccination. At first, she paid no attention to it, but when it began to enlarge she consulted a physician on the laboratory staff, who referred her to Dr. Winfield.

At that time, the lesion was an indurated nodule with a necrotic center elevated about one-eighth inch above the skin. A tentative diagnosis of pyogenic granuloma was made and treatment for that condition was instituted. In about a month the necrotic center had cleared up and the elevation was considerably lowered, but since that time there had been little change, except that the induration had grown larger and deeper.

The case was presented for diagnosis—although the suspicion of tuberculous granuloma was entertained—and for suggestions as to treatment.

DISCUSSION

Dr. Fordyce inclined to the suggestion of tuberculous trouble.

Dr. Williams thought it was a tuberculous lesion and that it should be excised. A definite diagnosis could then be made by microscopic examination of the specimen.

Dr. Highman agreed with Dr. Williams that it was a tuberculous nodule and should be excised.

CASE FOR DIAGNOSIS. Presented by Dr. Lane.

W. R. V-D., a man of 30, born in New Haven, a chauffeur, had lesions that were impossible to describe in detail as they were of so great variety, but it was hoped to make a detailed study of the patient later. He had been seen only once, a few days before. There was a generalized eruption on nearly the whole body. except the face and scalp. It started twelve years before as a general redness on the inner side of the right thigh, and had gradually progressed, developing symmetrically. It was most marked on the inner side of the thighs, the legs—front and back—the front of the arms and adjacent portions of the chest, and the back of the forearms. The most prominent characteristic was a marked telangiectasia, and in the centers of the larger patches, atrophy without induration. There were healed and unhealed ulcerations in the center of the patches on the right thigh and leg. On the areas where the lesions were new, there were small red spots at the sites of the hair follicles which at a distance gave the appearance of pityriasis rubra pilaris. There was no keratosis, the skin being perfectly free over these areas, but there were no hairs on them. A specimen of blood had been taken for a Wassermann test, but the report had not been received. The blood count was practically normal. Physical examination showed nothing except a soft systolic murmur at the second right interspace.

DISCUSSION

Dr. Whitehouse said he could throw no light on the case. There was no question of the angiomatous character of the lesions. It conformed to the type of angioma serpiginosum, but was associated with atrophy. It was altogether unlike anything he had seen. The ulcerations on the leg were peculiar.

Dr. Highman said it was one of the most significant cases presented before the Society during the year. In some respects it suggested angioma serpiginosum, but in other particulars it seemed like Majocchi's disease. It also reminded him of Stoke's case of specific telangiectasis. The association of distinct ulcerations made him wonder whether the entire group of capillary lesions of the skin might not be closely related to similar processes in the larger vessels supplying the tissues subjacent to the skin. That was an impression he had had for a long time, and it seemed to be corroborated in this group of cases. Raynaud's disease, and even Buerger's disease, might represent differences of degree and not of kind. This case opened up a new field of thought.

Dr. Howard Fox thought that the greater part of the eruption closely resembled angioma serpiginosum. He was unable to account for the ulceration.

Dr. Wise agreed with those speakers who thought that the case resembled angioma serpiginosum, but there were so many features of the eruption that differed from those of angioma serpiginosum that he did not believe that to be the correct diagnosis. He made the diagnosis of poikilodermia vascularis atrophicans (Jacobi) and exhibited the article and the cuts referring to that disease in the *Ikonographia Dermatologica.*

Dr. Winfield agreed with Dr. Wise and others who thought the case resembled angioma serpiginosum.

THROMBO-ANGEITIS OBLITERANS. Presented by Dr. Wise.

A man, referred by Dr. Mandelbaum, aged about 38, had had the condition for ten years. It began as a small ulceration between the fourth and fifth toes of the right foot, which was operated on and removed with some involved bone. The ulceration presented was of three years' duration and was located on the dorsum of the foot. The patient suffered intense pain at all times, and was presented for consultation in regard to the advisability of amputation and if so, the best site for it. The small toe had been amputated and a part of the metatarsal bone at the same time. Dr. Leo Buerger had paid quite a little attention to the patient at one time but it was not known what advice he gave the young man—whether to leave it alone or to have an amputation.

DISCUSSION.

Dr. Winfield said that the higher the amputation was made the better.

Dr. Fordyce recalled a case of Buerger's disease in which the patient had lost one of his toes. The Wassermann reaction was negative, but in spite of the blood findings the man was put on antisyphilitic treatment. Later the Wassermann reaction became positive. This was the only case of the kind he had seen in which the Wassermann reaction was positive. The patient developed no trouble after persistent treatment.

Dr. Williams said that the man had been under his care at the Skin and Cancer Hospital, and had improved for a time under large doses of potassium iodid.

Dr. Highman spoke of recent reports from Japan to the effect that these cases clear up at the seashore with wet dressings of sea water and exposure to the general tonic of the seashore life. Whether such treatment would be of any value in this instance, he did not know.

TATTOOING. Presented by Dr. Howard Fox.

N. A., an Armenian girl, 14 years of age, three years before, during the war, had been captured by the Turks and forced to become an inmate of a Turkish harem. As a brand of ownership, various bluish marks had been tattooed on her forehead, nose, temporal regions and chin.

DISCUSSION

Dr. Pels (by invitation) said that he had had some results with the desiccation treatment, using a unipolar method. Under local anesthesia and employing a fine operating needle, the destroyed tissue was subsequently removed with a small curet, at least as much as possible. The wound was permitted to heal up under aseptic conditions. The entire pigmented area, however, could not be destroyed without leaving much scarring, but under these conditions the cosmetic result was fair, and there was a resultant smooth scar which had a more satisfactory effect than the tattooing.

APHTHOUS STOMATITIS OF TWENTY-THREE YEARS DURATION. Presented by Dr. Howard Fox.

M. R., a man, aged 36, born in the United States, had several brothers and sisters who had suffered at times from a condition similar to his but in a much milder form. As a child he had had measles, mumps and frequent attacks of sore throat and frost bite of his toes. Since adult age he had suffered from dry pleurisy several times. On one occasion he passed a large amount of mucus from the bowel, which was seen by a physician. In the spring of 1918 he was treated at the Johns Hopkins Hospital for two months, a diagnosis of mucous colitis and aphthous stomatitis being made. The present disease began at the age of 13 and had continued to the present time. He had had a half dozen attacks yearly, lasting from two weeks to two months. The longest period of freedom from lesions of the mouth was six months. According to his statement, the sores in the mouth appeared either singly or as many as a half dozen at one time. They began as "pimples," soon becoming open sores, which were more or less painful, especially at the beginning. At times they interfered with sleep and caused thickness of speech. His appetite was poor, his bowels were constipated and he often suffered from marked flatulence. The patient appeared to be in fair health. He was of medium height and weighed 130 pounds.

At the time of presentation, the lesions, with the exception of a small superficial ulceration on the mucous surface of the upper lip, had temporarily disappeared. When seen six weeks previously, he presented four ulcerations of the mouth, two on the mucous surface of the upper lip, one on the buccal mucous membrane, opposite the last molar and one on the anterior pillar of the fauces. The size and depth of the ulcers increased in the order above mentioned, that on the fauces being dime sized. They were all moderately deep with elevated, angry red looking borders and yellowish centers. They were quite tender to the touch.

The obstinacy of the case was shown by a letter from the patient's brother, a well known physician, who said that "he had consulted many physicians and had been the subject of innumerable examinations, bacteriologic and pathologic surveys, blood counts, etc. So far he had resisted all efforts, medical, physical, psychic, hygienic, climatic, etc." The Wassermann reaction had repeatedly been negative and there was no history of syphilitic infection. There had been no improvement from either mercury or arsphenamin. Examination of the teeth showed no apical infection. The uric acid and sugar contents of the blood were normal; there was no evidence of acidosis on testing the alveolar air. A section of one of the ulcers had been histologically examined and the following report made by Dr. Pels: "There was a very cellular granulating tissue, some edema and fairly numerous collections of red blood cells; numerous infiltrating cells which consisted chiefly of small mononuclear leukocytes and a few polymorphonuclear cells. There were a fair number of newly formed blood vessels, and in some areas there appeared to be whorls of new connective tissue around the small blood vessels. There were also a few epithelioid cells."

As the examination of the stool had shown it to be "highly acid and extremely toxic," he was given a series of implantations of live colon bacilli, preceded by a series of alkaline enemas. While the patient was now nearly free of lesions, it was of course impossible as yet to say whether the improvement was due to the intestinal treatment, owing to the spontaneous disappearance of all of his previous attacks.

DISCUSSION

Dr. Isaac R. Pels (by invitation) said that the case had been one of considerable interest. The patient was seen a little over two months before and then had a number of ulcers on his tongue a little to the left—one on the right tonsil, and a large one on the right upper lip. In appearance they were all practically the same as the largest one on the lip, which measured approximately 1.5 cm. in diameter. They were characterized by a redundant appearance of the granulation, were sharply defined, rounded with no undermining of the edges, and a grayish-white granulation tissue which had no tendency to bleed. Scrapings made from this ulcer showed in two specimens merely what was considered foreign material, probably cotton or gauze fibers, and no definite mycelium. More complete examination showed nothing definite. The tonsils were fibrosed and cryptic, the tongue slightly coated, the teeth in fair condition. All the glands under the lower jaw were palpable, and there was distinct evidence of Fordyce's disease, especially on the lips and pillars of the tonsils, as well as on the mucous membrane of the cheeks. The biopsy specimen showed nothing distinctive, merely a picture of granulation tissue with active proliferation of the fibrous tissue. Dr. Pels said that his impression was that the condition was probably due to some metabolism deficiency or to some condition similar to the mechanism of herpes zoster, or to a combination of the two. As the patient had been under observation for only a brief time, a complete medical survey had not been made. This, together with a special study from the standpoint of tuberculosis, would seem to be the line of investigation to be followed.

Dr. MacKee said that he had obtained cultures of both the streptococcus and staphylococcus in such cases; also, that he had tried autogenous vaccines without favorable result.

Dr. Fordyce said that several cases of this kind had come under his observation during the past ten years. He had been unable to find any description of the condition except in Sutton's "Diseases of the Skin," in which it was described under the name of periadenitis mucosa necrotica recurrens. In his experience, the lesions have begun as small papules which rapidly break down and leave a small excoriated ulcer. They occur on the tongue and on various parts of the oral mucosa; they heal in about ten days or two weeks and almost invariably recur. He had one patient who had suffered from these lesions for many years; in addition to the mouth lesions, she had lesions on the vulva. This patient said that her mother and other members of the family had been similarly afflicted. The possible association of the condition with tuberculosis had suggested itself to him, and he had thought that the lesions on the mucous membranes were perhaps analogous to the papulonecrotic tuberculid seen on the skin. This, of course, was only a suggestion, as he had no direct evidence to support this theory.

MORPHEA GUTTATA. Presented by Dr. George H. Fox.

The patient, Mrs. S., exhibited an eruption, chiefly on the neck and waist and beneath the breasts. It began a year ago, near the vulva. The lesions were numerous and small, from pinpoint to split-pea size. Many showed a marked border and some showed a flat scaly surface. Some isolated papular lesions had a crusted center or one that was pitted, resembling lichen planus lesions, but there was a tendency of the lesions to coalesce and form linear or irregular ivory-like patches with the characteristic dry crinkled surface of morphea. There were no subjective symptoms and no family history, nor any apparent cause for the condition. During the past six weeks the patient's general condition had improved under diet and daily exercise.

DERMATITIS DYSMENORRHEICA. Presented by Dr. Wise.

A matron, aged 30, who had been referred by Dr. Katz, stated that she had had an eruption on the face and left breast with each menstrual period for the last two years. The eruption consisted of slightly edematous erythemato-vesicular patches which were somewhat painful. There was no evidence of its having been artificially produced. When the eruption disappeared it left a slight pigmentation, with a fading brownish hemorrhagic punctum in each follicle. Gynecologic examination revealed nothing but a tear in the cervix. She had been referred to Dr. Casamajor for consultation. He stated that the matter of psychoneurosis must be held under consideration, and that he did not believe the eruption to be self-inflicted.

DISCUSSION

Dr. Whitehouse said that in spite of the apparent phlegmatic temperament of the patient, he was inclined to consider the lesion a factitious one.

Dr. MacKee expressed the opinion that it was malingering, the result of hysteria associated with menstruation. The woman became hysterical at the time, and probably did not realize that she had injured the skin.

Dr. Howard Fox thought the eruption was self-inflicted, the lesions looking as though the patient had used sandpaper on her face.

Dr. Wise said that in five cases described by Matzenauer and Polland these authors demonstrated that it was not an artificial dermatitis, not self-inflicted. Dr. Casamajor had examined the woman and had been unable to elicit any history suggestive of an artificial dermatosis.

It seemed to be a spontaneously appearing condition appearing coincidentally with the menstrual period, identical with the eruptions described by Matzenauer and Polland.

Note: This case will be described in detail later.

A PECULIAR PAPULAR ERUPTION OF THE AXILLAE. Presented by Dr. Trimble.

A young woman, aged 29, born in Ireland, had in both axillae, especially on the anterior folds, great numbers of small papules about the color of the normal skin. These itched intensely. The duration of the trouble was three years, and it had slowly progressed from the beginning. The case was similar to the ones presented by Drs. Fox, Fordyce and others several years ago. The papules were about the size of the head of a small match and although situated close together, they were all discrete.

DISCUSSION

Dr. Fordyce said that since his observation of the original case described by Dr. Fox, he had seen a number of patients with this trouble. The sites of election are the axillae, the skin about the nipple and the suprapubic region. The lesions are noninflammatory and usually light red or yellowish in color; they itch intensely and are resistant to most of the ordinary antipruritics. Histologically, there is a marked hyperplasia of the epidermis, chiefly about the sweat duct orifices. The sweat coils below the epidermic lesions are greatly dilated. It is impossible to say whether the epithelial change is the result of an irritant from the sweat glands or whether the change in the sweat glands is due to a primary epithelial change.

Dr. Whitehouse agreed with one or two of the other gentlemen who observed that the axillary space was free from papular infiltrated lesions, and said it hardly seemed analogous to the cases reported under the title mentioned.

Dr. Highman remarked that the lesions in the case suggested the type described by Jadasohn as lichen trichophyticus, and he referred to Ormsby's paper and some European writers who spoke of aberrant forms of tinea, of which this case might be an example.

Dr. Howard Fox said that the eruption, which was not confined to the axillae, appeared to be an ordinary, thickened, intensely itchy patch of lichenification.

Dr. Lane thought the case was one of typical neurodermatitis with spots in a rather unusual location. The symmetry was also rather unusual. This diagnosis was still further borne out by the presence of a smaller typical patch of neurodermitis in the usual location on the nucha. He could see nothing to make Dr. Highman's suggestion of trichophytosis appear probable, although at present one did not dare to be positive on that disease before scrapings and cultures had been examined. The thickened skin, the exaggerated normal lines of the skin and the flat shiny papules were all characteristic of neurodermatitis and not of trichophytosis.

KELOID WITH GANGRENOUS CENTER. Presented by Dr. Trimble.

A woman, aged 32, born in the United States, had a keloid over the sternum which was operated on in October, 1919, by excision. The wound partially healed by granulation and was afterward skin grafted. The lesion returned, covering a large area, and showed a small keloid in each stitch hole. The interesting feature about the case was the small gangrenous adherent slough about the size of a hazelnut; it had not yet been ascertained to what this was due.

MILIARY TUBERCULOSIS OF THE FACE. Presented by Dr. Trimble.

A mulatto woman, 23 years of age, born in the United States; had an eruption consisting of a number of round lesions—pinhead to match-head in size—scattered over the face and particularly on the vermilion border of both lips. The lesions were translucent, and some of them had a central depression or indentation. At the inner canthi of both eyes the lesions had coalesced, making a small group. The patient was also suffering from some eye trouble which had been diagnosed as metastatic choroiditis. The eruption on the face had lasted about one year. Biopsy showed the lesion to be a granuloma.

DISCUSSION

Dr. Howard Fox said that the lesions on the nostrils were suggestive of lupus vulgaris. The eruption was similar to that of two cases (both patients were colored women) that he had recently presented, and he thought it certainly belonged to the class of disseminated lupus vulgaris.

Dr. MacKee said that this patient had been seen at the Vanderbilt Clinic about two years ago, and a microscopic examination then showed a typical tuberculous structure. At that time the condition yielded promptly to roentgen-ray treatment. The diagnosis was miliary tuberculosis.

EPITHELIOMA LINGUAE. Presented by Dr. Wise.

A woman, aged 50, presented a lesion on the left side of the tongue, of three months' duration. It was an irregular ulcer, 1 cm. in diameter, with a rather dirty base. There were no palpable lymph nodes in the neck. A pathologic report had not yet been received. The patient was presented in order to obtain some suggestions as to the proper procedure in the case—whether to refer her to a hospital for immediate operation or to wait until further information had been secured as to the nature of the lesion.

DISCUSSION

Dr. Fordyce suggested that the lesion might be tuberculosis of the tongue. He cited a case which resembled this one very much, in which the lesion was excised and found to be tuberculous.

Dr. Wise said the point referred to by Dr. Fordyce was the reason for presenting the case, for they had rather feared to make a biopsy. Would Dr. Fordyce approve of taking out a section?

Dr. Fordyce said that a wedge-shaped piece should be removed, taking out the whole of the lesion.

Dr. Highman said that in making a diagnosis of a lesion suspected of being epithelioma of the tongue, the excision should be made at a hospital, and while the patient is still narcotized a frozen section should be studied. If it proved to be epithelioma, the operation should proceed at once without waiting two or three days.

Dr. Fordyce said that the case should be treated just as are similar conditions in breast carcinoma, and if a frozen section were proper there it would be proper here. It is a routine procedure in all of the hospitals.

PSORIASIS OF THE PALMS TREATED BY ROENTGEN RAY: QUESTION OF DOSAGE. Presented by Dr. Howard Fox.

H. M., a schoolboy, 11 years of age, had suffered from psoriasis on different parts of his body for nine years, and on the palms for the past five years. He was shown to aid in proving the presenter's opinion that the small doses of roentgen ray, ¼ Kolzknecht unit (skin distance), were not as effective as larger doses in treating psoriasis. The boy had been recently shown at the Manhattan Dermatological Society, at which time Dr. Wise stated that he had given the patient fourteen weekly treatments of ¼ Holzknect unit by roentgen ray. There was no perceptible improvement, and the case was considered to be roentgen-ray resistant. During the past ten weeks, Dr. Fox had given the patient 1 Holzknecht unit to one palm and ½ Holzknecht unit to the other, and concluded that the best results in this case were obtained from ½ Holzknecht unit given every two weeks. The large dose, given twice at monthly intervals, caused the lesion to clear up, but it relapsed partially. The half unit doses were given to both hands. As presented, both palms were practically smooth. He had previously been treated by chrysarobin, without benefit.

DISCUSSION

Dr. Wise said that Dr. Fox had demonstrated his point in this case, but whether the same treatment would result so beneficially in other similar cases he greatly doubted.

Dr. MacKee agreed with Dr. Wise. In an extensive series of cases of psoriasis, when the lesions on one side of the body were treated fractionally and the lesions on the other side were treated intensively or semi-intensively, there was little difference in the results noted. On the whole, and for reasons that would require a long explanation, fractional treatment gave the best results and was the method of election. In these experiments, the total amount of ray administered in a month was the same with both methods. The speaker agreed with Dr Fox that one large dose (suberythema dose) would at times clear up psoriatic lesions that had failed to improve under the influence of fractional treatment, but this was not the usual phenomenon in his own experience. He was opposed to intensive treatment or to prolonged fractional treatment in a benign recurring disease, such as psoriasis, because in time the skin was likely to become dry from atrophy of the sweat and sebaceous glands, atrophic from changes in the connective tissue, and finally keratoses and other undesirable and even dangerous sequels might develop. If the lesions responded to a few fractional treatments and the patient remained free of eruption for a long period, such treatment was indicated; but if the eruption was or became recalcitrant, or new outbreaks were frequent, roentgenization in any form was contraindicated.

Dr. Whitehouse said he did not like to bring up a point that seemed like criticism, for he had great respect for the results of roentgen-ray treatment and what the speakers had done with it in certain distinct lines, but why should any case of psoriasis be treated with roentgen rays? He had never seen an eruption of psoriasis that could not be removed otherwise; and why should a generalized recurring eruption with a constitutional cause be treated with roentgen rays?

Dr. Howard Fox said that from his own experience he had for a long time felt that the larger doses had a better effect in psoriasis than the smaller ones.

He had expressed that opinion at a recent meeting at which the patient was shown, and the result had proved his contention in this particular case.

Dr. MacKee replied that one reason was that, as a rule—not always—the eruption would clear up more quickly than under any other therapy; another reason was that the patients preferred such treatment as they did not have to use disagreeable ointments. At the clinic, it was a rule that if the psoriatic lesions failed to clear up under three treatments of ¼ skin unit per week, some other method of treatment was instituted.

Dr. Whitehouse cited a case of symmetrical psoriasis that had been present on the forearms for seven years, which disappeared under one application of Vienna paste: salicylic acid, 20; chrysarobin, 20; oil of birch tar, 10; anhydrous wool fat, 25; soft soap, U. S. P., 25. The patient had a severe generalized dermatitis, but a second application was not necessary. The patches were sharply defined and infiltrated and had been present seven years.

Dr. G. H. Fox, referring to the test of using strong exposures on the lesions on one side and weak exposures on those of the other, said that it was impossible to cure half of the body of psoriasis. If you cure one side, the other side will soon get well spontaneously. A marked contrast of the two sides of the face can be produced by treating one side alone in acne, but this cannot be done in psoriasis.

Dr. Highman said that there were other points that might be brought up by Dr. Whitehouse's inquiry. As Dr. MacKee said, roentgen-ray treatment was cleaner, pleasanter and cheaper, and the patients preferred it. It was most convenient to the patient in regard to time, expense and pleasantness.

Dr. Howard Fox said he was speaking more particularly of psoriasis of the palms. The patient had previously been treated with chrysarobin by a well-known dermatologist.

Dr. Fordyce was opposed to the use of roentgen ray in treating generalized psoriasis unless the rays were employed by one thoroughly versed in modern technic. He had seen many cases of telangiectases following the use of the roentgen ray for this trouble.

Dr. MacKee said that Dr. Whitehouse's remarks were pertinent. The solution was not to carry roentgen-ray treatments too far. The skin would tolerate a certain amount of the rays (¼ skin unit per week for several weeks) without showing microscopic alteration. Even with slight changes, such as retardation of physiologic activity, there would be complete regeneration to the normal. It was safe, therefore, to administer a course of a few fractional treatments, and such courses might with safety be repeated occasionally over a number of years. No harm would be done so long as the dose was sufficiently small and the doses were not administered too close together.

Dr. Winfield asked whether it would not be better not to educate these patients to go to roentgenologists for treatment, since if they fell into the hands of men who were not dermatologists or roentgen-ray therapists, great harm might be done in the future, and the end results might be far more serious than the original disease.

Dr. MacKee said that in many instances a psoriatic eruption would disappear under the influence of the roentgen ray and the patient would remain free of eruption for months or even years—not by virtue of the roentgen ray, but for unknown reasons. Conversely, it was not infrequently observed that the patient developed immunity against the beneficial influence of the roentgen ray, which, in a way, is a protection for the patient. In such instances the roentgen ray should be discontinued.

It seemed to the speaker that the roentgen ray, if properly employed, was a good treatment for many cases of psoriasis, especially selected cases.

Dr. G. H. Fox said that a few years ago he made a diagnosis of dermatitis herpetiformis in the patient, but tonight he was reminded of cases seen by the hundreds fifty years ago in Hebra's clinic—cases of prurigo. The colorless nodules and the dry excoriated skin made it a perfect picture of what Hebra would have called prurigo.

Dr. Fordyce said that this case impressed him as one of prurigo. The lesions presented were very much like the typical prurigo papules.

Dr. Howard Fox said the eruption had been puzzling on account of its frequent changes in appearance, at one time resembling dermatitis herpetiformis, at another erythema multiforme, and at another prurigo. As yet he had not been able to influence the course of the eruption though many methods of treatment had been tried.

Dr. Williams inquired whether the child had been examined for local infections.

Dr. Fox replied that her teeth had been examined with the roentgen ray and no apical abscesses discovered. Her teeth had been put in good condition by a dentist. There was no source of infection in the tonsils. She had never suffered from attacks of sore throat.

Dr. Winfield said that while the case certainly looked like prurigo tonight, he had no doubt it was a case of dermatitis herpetiformis.

Dr. Highman asked how many times tonsils had been examined for focal infections when there were no dermatoses.

MELANOMA TREATED BY RADIUM. Presented by Dr. Clark.

Miss R., aged 35, born in the United States, as long as she could remember, had had a small, slightly raised dark mole on the outer surface of the upper part of the left forearm, about the size of a split pea. She had noticed no change in this lesion until about eighteen months ago, when, without apparent cause the lesion began to grow rapidly.

When first seen, six months before, the lesion was the size of a 50-cent piece, was distinctly raised, and the surface was warty with a scabbed condition over the central part. It would bleed whenever it was bumped or the scab disturbed. Neither the epitrochlear nor the axillary glands of that side showed any enlargement. After consultation with surgeons, it was advised that a massive dose application of radium be made to the lesion. Because of its size, it was necessary to divide the area in order that the applicator might cover all parts, and an extensive exposure was made in this manner. A marked reaction resulted, followed by a heavy rupial covering. At the end of about eight weeks, the crust came off, and it was then noticed that there were still signs of the black melanotic lesion over the center of the exposed area. Another massive dose application was made, not as prolonged as the first, which was followed by a superficial ulceration and crusting. This crust came off six or seven weeks ago, leaving a small raw area in the center with three black melanotic spots around its edges. Since that time these melanotic spots had diminished in size almost to the point of disappearing, but the central superficial ulcerating area had shown no signs of healing. It gives a hot and burning sensation and when left dry tends to become covered with a scab with a superficial crust. The patient showed no glandular enlargement.

PAPULONECROTIC TUBERCULID. Presented by Dr. Wise for Dr. Fordyce.

Y. J., a schoolgirl, aged 13, an American, exhibited an eruption which had been present for six years—lupus erythematosus on the scalp and nose, and a papulonecrotic tuberculid of the face, hands and arms. The lupus erythematosus involved the entire nose and on the scalp was present in patches from 1 to 5 cm. in diameter. The typical redness, adherent scale and telangiectasia were present, and the scalp lesions exhibited considerable atrophy and alopecia. The cheeks and both sides of the hands were the site of a papulonecrotic tuberculid with many dusky red papules from 1 to 5 mm. in diameter, interspersed with the pitted scars of previous lesions. The forehead, too, showed a few scars of acnitis, and the fingers had the frost-bitten appearance seen in lupus erythematosus. The histologic examination of one of the papules proved it to be a papulonecrotic tuberculid.

ALOPECIA TOTALIS. Presented by Dr. Schwartz.

The patient was a boy of 11 who had suffered from the condition exhibited for two years.

PAPULONECROTIC TUBERCULID. Presented by Dr. Wise for Dr. Fordyce.

F. F., a Russian girl, aged 11½, had lived in the United States for ten years. She presented a papulonecrotic tuberculid of five years' duration, occupying the face and the extensor surfaces of the arms. There were found the typical small violaceous papules, from 1 to 5 mm. in diameter, each having a minute greenish-white central necrotic point. The usual small pitted scars were intermingled with the papules.

PARAPSORIASIS LICHENOIDES. Presented by Dr. Wise.

An expert mechanic, aged 35, born in Holland, had been referred to the speaker by Dr. Wallhauser of Newark. When first seen, he presented an extensive eruption involving the arms, legs, thighs and neck. The lesions, which were numerous, were dusky red papules from 3 to 10 mm. in diameter, with a faint scaling. The duration of the condition was two years, and none of the lesions had disappeared. He received ¼ unit of roentgen-ray treatment weekly, and after six or eight weeks of treatment the improvement was 60 to 70 per cent. The lesions were not now so distinct as when Dr. Wallhauser had showed the case before another society about two months ago. Some had disappeared completely, others had faded to faint brownish macules.

MYCOSIS FUNGOIDES. Presented by Dr. Wise for Dr. Fordyce.

F. E., aged 34, had previously been presented at other meetings with the diagnosis of possible mycosis fungoides and a tentative diagnosis of parapsoriasis en plaques. The patient also had alopecia and the hair became gray in patches. Dr. Fordyce did not present the case with the idea that the three conditions were related. A biopsy had been made and examined by several pathologists, none of whom decided on the diagnosis of mycosis fungoides. Dr. Pollitzer had called the speaker's attention to Darier's opinion, saying that diagnosis in an early case is impossible, and the clinical diagnosis—whether mycosis or parapsoriasis—was still undecided. The duration of the condition was eight years. The patient did not complain of much itching.

LICHEN PLANUS IN THE MOUTH. Presented by Dr. Wise for Dr. Fordyce.

A young man exhibited lesions of the buccal mucosa which extended along the interdental line. There was a fine lacework of milky color, but no individual papules could be discerned. Subjective symptoms were entirely lacking and for this reason no history of the duration could be obtained. Lichen planus was the tentative diagnosis, no biopsy having been made.

URTICARIA PIGMENTOSA (ADULT TYPE). Presented by Dr. Wise for Dr. Fordyce.

J. F., a native of the United States, aged 42, a teamster, had a brown macular eruption of fifteen years' duration. The trunk was especially involved, and the rest of the body as well, except the face, hands and feet. The macules ranged from 1 to 7 mm. in diameter and when briskly rubbed were transformed into temporary wheals. A biopsy had been made, but the laboratory report had not yet been received. The patient stated that the eruption had appeared immediately following a chancre fifteen years previously. The Wassermann reaction was + + + +.

CHROMOPHYTOSIS FOLLICULARIS. Presented by Dr. Wise.

I. R., a negro, aged 22, from Dr. Fordyce's clinic, was presented to show a rather unusual type of chromophytosis. There were faintly scaling macules over the clavicles and numerous follicular and lichenoid lesions. A scraping showed the typical fungus of chromophytosis.

DERMATITIS HERPETIFORMIS. Presented by Dr. Howard Fox.

A. M., a girl, 9 years of age, born in the United States, had previously been presented before the Manhattan Dermatological Society on April 13, 1918. The case presented two special points of interest: first, the occurrence of the eruption ten days after vaccination for smallpox, and second, the changing type of the eruption from time to time. The disease had existed for five years and with the exception of a remission for two months last summer, she had never been free from lesions. At present the eruption was mostly confined to the extensor surfaces of the forearms and presented shotty papules with an intense pruritus that closely simulated prurigo. On some previous occasions a picture of erythema multiforme with typical iris lesions was presented that would have been classic except for the presence of some excoriations. On other occasions during the past three years she had shown a typical eruption on the face, trunk and extremities of the papular type of dermatitis herpetiformis.

Efforts to ascertain the cause of the eruption had been unavailing. A physical examination by Dr. Longcope revealed nothing abnormal, except the eruption. Blood examinations were negative. Roentgen-ray examination of the tonsils and teeth revealed no evidence of focal infection. Cutaneous tests with twenty-six proteins were negative to all except coco and cornstarch. Salves containing the latter substance were accordingly omitted, but no change in the patient's condition resulted. Examination of the stools showed them to be highly acid and extremely toxic with absence of colon bacilli. She was therefore given treatment by implantations of live colon bacillus, preceded by a series of alkaline enemas but there has been no improvement up to the present time.

PSORIASIS IN A DIABETIC ON STARVATION DIET. Presented by DR. HOWARD FOX.

J. K., an ex-soldier, 22 years of age, born in the United States, was shown through the courtesy of the U. S. Public Health Service. He had suffered from diabetes mellitus for the past six months, and at the time of presentation the urine contained 3 per cent. of glucose; he had lost 50 pounds since the beginning of his illness. He had been given the Allen (starvation) treatment. Five weeks before he presented a profuse eruption of typical guttate and nummular psoriasis of the scalp, trunk and extremities and a slight eruption on the face. The eruption was the first of the kind from which he had ever suffered.

SPOON NAILS (KOILONYCHIA). Presented by DR. HOWARD FOX.

J. W. C., a man, 26 years of age, born in the United States, a clerk, had a negative family history, none of his relatives having suffered from disease of the nails. As a child he had had scarlatina, diphtheria and measles. He was married seven years before presentation and had two apparently healthy children. Five years ago, subsequent to the birth of his children, he contracted syphilis and was treated by a well-known dermatologist. The Wassermann reaction at present is negative. He had at one time been a heavy whisky drinker. He was of nervous temperament and bit his nails frequently. The affection of the nails first appeared a little over a year ago, symmetrically affecting the thumb, index and middle finger nails of both hands. Examination showed a spoonlike hollowing of the distal two thirds to three fourths of these nails. The free ends were tilted upward, were brittle and showed a slight ungual hyperkeratosis. There was a lessening of the normal luster of the nails, the color not being markedly changed. There was no evidence of paronychia. The toe nails were not affected.

DIFFUSE SCLERODERMA. Presented by DR. HOWARD FOX.

S. N., a man, 22 years of age, born in the United States, a machinist, with a family history that was not significant, had suffered from scarlatina and measles in childhood. He had at one time been a great cigaret smoker. He denied venereal disease and did not drink alcohol. He had had a severe attack of pneumonia in the fall of 1918, from which he had made a slow convalescence. Previous to this attack his general health had always been good. The present illness began about two months after the attack of pneumonia, the patient first complaining of severe sharp pains in the knees when walking. This continued for about a month. He also suffered from attacks of vomiting which had continued every day up to the time of presentation. The attacks were severe at first, occurring after every meal and frequently between meals. At present they occurred only in the evening. He had lost 35 pounds since the beginning of his illness. He gave no history of cough or other symptoms suggesting tuberculosis.

He was poorly nourished, 5 feet 8½ inches in height, and weighed 114 pounds. There was a general firm, hard symmetrical, hidebound condition of the face, trunk and extremities. This was most marked in the hands which were cold and bluish. They showed a few small areas of vitiligo, some of them on previous sites of warty lesions removed by acid. There was no evidence of an associated Raynaud's disease. There was partial ankylosis of the joints of the fingers and wrist. The fingers, though stiff and hidebound, did not show pronounced tapering of the ends. The involvement of the cheeks made the face expressionless. The hair was dry, thick, brown and curly. The nails were normal. There was a good deal of dirty, yellowish-brown pigmentation, particularly on the trunk. There was a band of pigmentation about an inch wide along the lower dorsal and lumbar region of the spinal column. There were also larger areas of pigmentation over the scapulae, shoulders, backs of the arms and buttocks and to a less extent on the thighs. In places there was a slight scaling as seen in ichthyosis. There was no change in sensation to touch, pain or temperature or muscular sense. The reflexes were not pathologic.

Examination of the eyegrounds showed "marked dilatation of retinal arteries of the same caliber as the accompanying veins." The mouth, throat and organs of the chest and abdomen were apparently normal. The Wassermann reaction was negative. The urine showed a few granular casts but was otherwise normal. The blood pressure was 100 systolic, 80 diastolic. Blood examination showed: red cells, 5,600,000; hemoglobin, 95 per cent.; white cells, 9,200. Differential count: polymorphonuclears, 70 per cent.; lymphocytes, 22 per cent.; large mononuclears, 4 per cent.; eosinophils, 4 per cent. Blood chemistry: urea nitrogen, 11.5 per cent.; creatinin, 2 per cent.; uric acid, 3.1 per cent.; sugar, 110 mg. Coagulation time was six minutes. Roentgen-ray examination of the sella turcica showed "small clinoidals nearly in apposition." The patient was being treated with thyroid extract.

SARCOID. Presented by Dr. Kingsbury.

A young woman with lesions on the cheek, suggesting erythema multiforme or a toxemia due to pregnancy, gave a history of having had a similar condition when pregnant four years previously. When presented, she was in the fourth month of pregnancy, and the lesions had been present for two months.

HYDROA VACCINOFORME. Presented by Dr. Kingsbury.

A girl, aged 9, gave a history of having had the eruption last year and again this year. On exposure to the sun one week before, the eruption had appeared on the legs and arms.

EPITHELIOMA OF THE FINGER. Presented by Dr. Kingsbury.

A man, who had suffered from psoriasis for fifteen years, had an ulceration on the finger that had been present for over a year. There were keratoses on the backs of both hands, and this ulcer began on one of them. The patient also had an ulceration between his toes.

LICHEN PLANUS. Presented by Dr. Kingsbury.

The patient presented papular lesions on the thigh and a linear dispersion of lesions on the chest.

Book Reviews

AN ATLAS OF THE PRIMARY AND CUTANEOUS LESIONS OF ACQUIRED SYPHILIS IN THE MALE. Charles F. White and W. Herbert Brown. London: John Bale Sons, 1920.

The authors had an opportunity to make photographs of selected patients from 19,000 cases of syphilis that came under their observation. One purpose in presenting a selection of their collection in the form of an atlas was to aid in the early clinical diagnosis of initial lesions.

The majority of the photographs are stereoscopic, and the three dimension illusion when viewed through the instrument makes a better visual impression than the flat presentation.

Short notes and descriptions of the lesions are given. The text is based on the experiences of the authors. Although they admit that any classification of syphilitic chancres is difficult because types merge one into the other, they give this list with percentages based on an analysis of over 9,000 primary sores.

Class of Sore	Per Cent.
Primary hunterian chancre	13.45
Primary granulating syphilitic sore:	
(*a*) Circular or oval	21.21
(*b*) Linear	0.26
Primary abrasive syphilitic sore	2.96
Primary papular syphilitic sore	0.79
Primary papulo-abrasive syphilitic sore	29.31
Primary ulcerative syphilitic sore	2.28
Primary phagedenic syphilitic sore	0.79
Primary meatal syphilitic sore	2.50
Primary intra-urethral syphilitic sore	0.08
Primary concealed syphilitic sore	26.37

Only 131 cases of extragenital chancre were encountered in over 19,000 cases, and twelve stereoscopic pictures are given of the various types and locations.

To aid in the clinical differentiation, a description and photographs of nonsyphilitic or soft sores is given. One out of four lesions were of this character. The practitioner is warned to be certain of his diagnosis before telling the patient that he suffers from soft sores only, as he may have a double infection, or the syphilitic infection may make itself evident at the site of the soft sore or elsewhere. The use of the dark field illumination method for the demonstration of the syphilitic organism is urged.

Following the section on cutaneous syphilis is a short presentation of skin lesions which not infrequently are mistaken for syphilis.

Four colored plates are included, which are good examples of this type of work.

The atlas is valuable and should appeal especially to those who have not had the opportunity of seeing many clinical cases of dermatologic manifestations of syphilis.

SYPHILIS IN CHILDHOOD. Leonard Findlay, M.D., D.Sc., F.R.F.P.S.G. London, Oxford Medical Publications, 1919. Pp. 150.

This is a clear, well written and exceptionally well printed book on syphilis in childhood, based almost exclusively on the studies of the author (some in collaboration) at the Children's Hospital of Glasgow and at the Medical School of Glasgow University.

Findlay believes that of the terms "congenital syphilis" or "hereditary syphilis" the former is decidedly the better. An organismal disease cannot in the true sense of the term be hereditary. "Hereditary" implies some peculiarity or characteristic inherent in the germ cells, and appearing in one generation after another. Syphilis does not conform to this law.

Numerous histories of maternal and paternal syphilis are given in the discussion, and indeed, these case histories to the number of forty-seven are well distributed throughout the twelve chapters. The presentation of a chapter on "Acquired Syphilis in Childhood" should stimulate consideration of this phase of the subject.

There are six colored plates, thirty-seven other illustrations in the text, and four charts.

The book is worthy of interest not only to the practitioner, but also to the syphilologist and pediatrician.

RECENT ADVANCES IN THE TREATMENT OF SYPHILIS. By Rajendra Kumar Sen, in charge of the Hospital and Dispensary of Dejoo Tea Co., Ltd. Cloth. Price, 3 Rs. Pp. 82. Calcutta: Butterworth & Co., 1919.

Sen presents the Prize Essay of the *Indian Medical Gazette* for the best paper on this subject. He gives an outline of the contributions toward the present knowledge of syphilis, quoting freely from the published articles of others. He includes his "Notes on Salvarsan" reprinted from the *Indian Medical Gazette* of August, 1914. Sen gives arsphenamin at intervals of four weeks, as he asserts that the drug given in doses of 6 dg. is not completely excreted even after three weeks.

The monograph gives no indication of the prevalence of syphilis in India. It is of no value to the syphilologist of this country.

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SOME THOUGHTS ON PRECEDENT *

MARTIN F. ENGMAN, M.D.
ST. LOUIS

To preside over this body which represents the most eminent in American dermatology is indeed an honor and one to which laudable ambition should aspire. I, no different in this respect from my peers, feel highly gratified that this office should have come to me and I wish to express to you, my colleagues, my gratitude and high appreciation. To preside over the annual convention of such an assemblage as that represented by the American Dermatological Association is not a hollow honor but carries with it responsibilities; responsibilities which nag one for many months before the day of culmination or execution. One of these, the most weighty, the one which has borne most heavily on this presidential crown, is the annual address.

In reading the addresses delivered by your presidents for many years back, it appears that of the subjects I might select, all have been exhausted: the history of this Association, its past and future have been well discussed; the journal—our pride—its history, its editors and shortcomings have been well discussed; the history of dermatology has been well discussed; so what is left for me but the broad field of dermatology?

I am sure there is nothing so interesting to dermatologists as skin diseases and their discussion, with the possible exception of golf, to some of our older and heavier members.

The presidential address is not limited as to time; the hammer of the presiding officer does not abruptly stop its flow; it may, like Tennyson's brook, babble on forever. And there is no prescribed limit to its scope; one may hurdle pedantic fences, hoary with precedent, and gambol in the glad sunshine of this liberty.

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* Presidential address read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

* Studies, reports and observations from the Dermatological Department of the Barnard Free Skin and Cancer Hospital and the School of Medicine; Washington University, St. Louis, Mo., U. S. A., Service of Drs. M. F. Engman and W. H. Mook.

The presidential address seems to act, at times, like one of those potent potions concocted during the middle ages to clear the system of humors. It seems to act in this way on the dermatologic system; it drives dermatologic humors, that have been stored up for years, to the surface.

With the glad feeling of liberty which you have thrust upon me in meeting assembled, I will open the gates to this large dermatologic field and will playfully gambol about in its patches of shade and sunshine; but I promise you I will return home long before the lunch bell rings. Whether you will receive proper invigoration by my exercise will remain a question.

Those who have given years of study to a special subject must finally come to the mental condition of those ancient Greek philosophers who, realizing the fallibility of all human knowledge, saw the impossibility of demonstrating truth even though truth be evident. One feels almost like Arcesilaus who, denying both intellectual and sensuous knowledge, publicly avowed that he knew nothing, not even his own ignorance. Experimentation and verification have been the two criteria of truth in its modern demonstration. To medicine these attributes have been as the wings of progress.

We who have been engrossed in the study of skin diseases for a quarter of a century or more must, if we have normal minds, realize our ignorance: how little we can possibly add to the chaos of things to be known, in the short space of a lifetime! To the novice the textbook and the printed page is as the chapter of Genesis was to the theologians of the middle ages—almost divine truth. But as the mind matures, considers and dwells on the fallibility of human knowledge, inquiry is awakened and often heresy results. Epicurus rightly taught that truth can never be determined by pure reason. The scientific trend of the modern mind demands and seeks experimentation for the verification of truth. This is not the trend of all modern minds, not the nature of all modern minds; the majority are probably pre-Platonic and do not reason from observed details to generalities.

Medical literature, especially dermatologic literature, is still carrying along on its many pages folk-lore, legendary data, obsolete theories and vague fancies, indelibly impressed on those pages by precedent. The same force—a virile potent force it is—has engrafted and impressed on the life of all ages and peoples, fallacies born of legend that centuries and centuries have nurtured.

The study of a science should not only be the acquirement of knowledge that has accumulated in the past, but inquiry into the truth of that knowledge and the demand of verification; and, if that is not satisfactory or sufficient for mental quietude, investigation anew to determine truth, is demanded. But how many of us assembled here have time to seek this goal? Our branch of science has not received that gift of the gods—endowments. We, the devotees, plod along the weary path of bread-earners, chained to the necessity of earning a livelihood, while we yearningly look into the unexplored fields of research as we pass along. Yet many here, and many others who have sat in this assemblage have, in moments of recess, delved into these alluring places and have blazed trails to many truths.

All fields of research are full of stubble, weeds and thistles, which from their very nature must be removed before truth can be found, yet knowing this we turn our novices into these fields, the books and literature on these subjects guiding them into false snares: guides which we, the older ones, have found false or inaccurate in many ways. In other words, we pass to our students through books, lectures and magazines, observations or data that have clung to our literature for many decades and which have not stood the test of time and verification. The history of a disease and its literary evolution is interesting and important; but why continue to place among the etiologic factors, for instance, data that at the present time bear no relationship to the disease in question, other than as a matter of history; and under "treatment" the results of folk-lore, legends and medical deductions based on false premises? Ideas and thoughts that have died years and years ago still haunt the pages of our literature. These ghosts stand out gauntly on many pages—emblems of precedent. Precedent is ever with us, menacing to some, acceptable and comforting to others; the greatest handicap to progress, the check to inquiry, the bugbear of the ages, the cloud which so frequently obscures truth. Khaliff Ali, the son-in-law of Mohammed, remarked that "in the course of my long life, I have often observed that men are more like the times they live in than they are like their fathers." We live in an age of inquiry and investigation and we, like the times in which we live, are investigators in a modest way. Inquiry and investigation have always been the undoing of precedent; they have riddled and destroyed false theories and beliefs that have held men's thoughts in iron chains for ages.

Realizing that precedent was the greatest handicap to dermatologic progress, and not being very reverential, some curious thoughts and heresies have come to me as a result of inquiry, sometimes verified by experiment, sometimes not. The same thoughts have no doubt occurred to others. Among these inquiries I have often thought of diet in skin diseases—why is meat and the nitrogen partition such a dreaded thing—why the cry in all diet lists—meat—beware of meat? Since Emil Fisher gave us those eighteen or twenty "building stones" of the protein molecule to play with, we have built many theories and have juggled these building stones about joyfully. Nature, it seems, can play havoc and cause many curious eruptions with these "stones." She can build subtle molecules which may slip by the best regulated and most careful intestine cells and cause all kinds of trouble. We do not exactly know the physical appearances of these troubles, but we feel that we have an intuitive knowledge of them; therefore, in order to be positive that such devilish juggling of building stones does not occur again or continue, we prevent the entrance of meat into the patient's body. We fear meat just as the ancients did, but we are not so discriminating as they were; in certain conditions they allowed only the food of animals that fed on certain shrubs or trees. Meat from old animals was said by them to produce foul and burning humors.

When man first became conscious that he was man, he was probably hanging from the limb of a tree with one foot, while he grasped a branch with another, and cracked nuts or ate fruit. He was a vegetarian. When the chilling blasts of the last glacial period drove him hungry and starving, south into the tropics, even there the cold had killed his vegetable foods; the vegetarian was forced to kill and eat his kind or another kind in order to live. He then became a meat eating animal. As he took his first bite of meat, did he begin feeding himself for kidney diseases, joint diseases and skin diseases? Did the serpent hand a tenderloin steak to Eve instead of an apple? Is there a mistake in the old Chaldean legend? Was this mastication of meat the birth of sin, disease and death? If not, why and on what ground of investigation and experimentation is red meat, animal protein, so interdicted in diet lists. Man has eaten meat for at least 240,000 years as estimated by learned anthropologists and ethnologists, and although many have died during that time, he, when not interdicted by his doctor or his purse or other circumstances, will still choose meat in preference to his anteglacial nuts.

Protein sensitization has come to our assistance and seems to be forming some order out of these chaotic ideas of meat diet. Focal infection has taken from the heterogeneous mass of diseases supposed to be due to protein diet, arthritis, rheumatism, certain forms of gout and certain skin eruptions. Haig's beautiful work on uric acid diathesis is one of the ghosts that still haunt the pages of medical books. The study of focal infections and protein sensitization are clarifying the cloudy obscurity of certain chronic kidney conditions. We must admit that learned and well thought out diet lists have been propounded for various diseases founded on precedent, to which the patient has been made to fit. So it is carried out today and will be tomorrow. The trend has been to make the patient fit the diet, and not the diet the patient. What a flood of light has been thrown into these dark recesses by the work of such men as Funk, Osborne, Mendel, McCollum, Goldberger and others. The chemical bodies contained in certain foods called "vitamines," so necessary to life's equilibrium, are probably the fundamentals of diet. How many diseases at present classified under obscure and numberless etiologic factors are due to unbalanced diets—diets in which a high protein intake is necessary, proteins or other foods taking with them those life and health giving, elusive chemical principles? How rapidly do the papulonecrotic tuberculids in children seem to disappear, together with the scrofulous glands under a diet rich in butter, cream, lamb and those foods known to contain growth vitamins! McCollum's book on the "Newer Knowledge of Nutrition" is an intelligent guide in this wilderness.

How many pathologic conditions are due to vitamin starvation, meat starvation, egg stuffing or milk inundation? What a great loss of energy is sustained in those cutaneous disorders in which almost the whole surface is inflamed and covered by scales with multiplied surfaces which increase evaporation and the dissipation of heat, as in the erythrodermas! How necessary, therefore, in these conditions is an increased intake of foods, nourishing and of high caloric value, such as alcohol, sugar and cream with meat and proteins for endurance and stability. How grateful to the patient is this increase of calories and how successful in keeping up the equilibrium for defense against intercurrent infections.

The intricate synthesis of lipoids and fats is still a physiologic problem, especially in dermatology with its Hebraic ideas about oily seborrhea. Is oily seborrhea due to an excessive intake of fat, or is it due to the small bacillus of Sabouraud? The Fucks-Hebra idea of seborrhea still stalks in our midst. Is it a disease; is it a dietetic disease? If a dietetic disease, on what evidence, except that furnished by precedent, is it classified as a dietetic disease? On what scientific evidence or verification or experimentation has this idea, as to its dietetic and hygienic origin, been established? The seborrheic state and its progeny—acne and the seborrheids—appear with those secondary sexual characters recognized as the dawn of puberty. The shiny nose of the high-school girl is as sure a sign of puberty as the little powder puff and silver vanity case. Some noses shine more than other noses, some skins ooze more oil than other skins, but by what standard or unit shall we pronounce disease? Shall we say the cause of this excessive cutaneous production of oil is the ingestion of fats, sugar, chocolate, candies and rich foods, because nature at that age demands such foods as butter and cream vitamins and those of high caloric value that can be easily burned? How do we know that acne vulgaris with the embryonic comedo is due to the rich food intake craved by youth? The microscope does not verify this old theory. It analyzes the acne lesion as one caused by the presence of a bacillus, always there just as a bacillus is always present in the tubercle of tuberculosis. Do chocolates, pancakes, pies, cake, sugar, fats and candies cause such a lesion? Can such a theory be verified by our general knowledge of histopathology? Can we assert that diet might cause directly or indirectly a lesion such as acne? But we have lesions similar to those of acne, due to the presence of organisms in the lesions. This fact we can use as a clue for verification. Oily seborrhea and the comedo are the insignia of youth and the dreams of puberty. Seborrhea is a type, the representative of a strain, a family. How the poets paint these types; they see them undisturbed by precedent.

Dickens paints Mr. Chadband with wonderful truth. How oily he was, how he beamed and oozed oil! Mr. Chadband, we know, must have had acne vulgaris in his youth—he had the scars of it. Was his oiliness a disease or a part of Mr. Chadband's nature? Was it a part of him, just as much a part of him as his nose with its large pores and thickened yellow skin? It may be that Mr. Chadband ate too many stimulating vitamins in his youth. Who knows? But is it not more likely that Mr. Chadband was of a strain, the result of Mr. Chadband's progenitors? To such skins as that presented by Chadband, Darier wishes to apply the term "kerosis"—recognizing it as a type or strain of individual.

As Buckle has pointed out, environment and diet form racial types and consequently racial natures; therefore, back in the dark recesses of history may lie the cause of oily seborrhea, the fundamental condition that furnished the soil for those seborrheic diseases so well portrayed by Sabouraud. Besnier, Audry and Darier see with the poet's eye the type of man who oozes oil, has acne, yellow skin and stringy, greasy hair.

Precedent has been one of the strongest outposts against the advance of inquiry into diet. Diet is elusive and mysterious, yet through inquiry light is being brought to bear, through diet, on that mysterious condition of the skin so often fought over and so elusive—eczema. Through a knowledge of sensitization, types, strains of men, environmental conditions, trades, occupations, histopathology and experimentation the eczema of our teachers, the eczema of too much meat, the eczema of the diet of the century past proves to be a ghost, a phantom, wrapped in the mystery of precedent.

The exudative diathesis of Czerny is a living type, living and pathetic; with enlarged glands, bronchial cough, oozing, scaly skin—on through life suffering, exudative! How we have followed precedent in the treatment and elucidation of these cases, until the study of sensitization brought the light. What truth was there in the past ideas of diet in these cases when fats, proteins or mineral salts were excluded? Some of these cases are now known to be due to wheat sensitization; some to egg, some to pollen, and others to bacterial sensitizations. How many young lives have been lost by intercurrent infections due to the lowered resistance of a restricted diet.

How interesting at the present time are all cases of so-called eczema, the solution of which means the employment of inquiry and investigation in each individual case, the flow of imagination, the pleasure of inductive reasoning, the joy of success. Life's work takes on a pleasanter phase and new vigor when one's own inductive powers can be used instead of the wise shake of the head with the printed diet list in the handling of acute, subacute or chronic eczema.

Soiling lotions, greasy salves, nauseous concoctions, starvation diets, quassia, gentian, alkalies, acids, arsenic may now be replaced by inductive reasoning, inquiry and investigation. How much longer will the ghost of eczema theories cling to our literature; how long the eczema diets of yesterday? How much longer will the urticarial lesions, the lesions of erythema multiforme, drug eruptions and others of this character be hung on the fibers of the vasomotor system? Histopathology has appeared to portray to us only a picture of morphology in the study of these eruptions, and it has been comforting to believe that somehow through the subtle influence of a "toxin" on the vasomotor system these eruptions occur; yet von Duhring, Phillipson and Gilchrist have told us of their purely inflammatory nature, of the wonderful biologic and chemical forces set in operation at the site of these lesions; however, we still take the comforting vasomotor view of all the eruptions of the erythema and urticarial groups.

Dermatology is a wonderful field for research and inquiry; a beautiful study and one that its devotees should love, for it contains so many wonderful things—things that fit into the very fundamentals of life. It is a constant source of inspiration. Its lesions, though on the surface of the body, are symbols which speak of deeper things, often of life's most obstinate and hidden problems; lesions significant often of trades, occupations, habits, customs, types, races, families, diseases lying deep in the system, dispositions, vanities, frivolities, physiologic periods; even flitting thought often leaves its impression as a blush or a lesion.

The skin and its digression from the normal is a study which should inspire one to employ all the forces of inductive reasoning, inquiry, investigation and experimentation in the search for truth—but truth shorn of precedent.

THE CHEMISTRY OF ARSPHENAMIN AND ITS RELATION TO TOXICITY *

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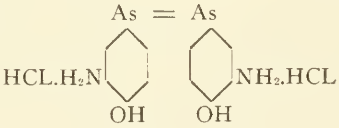
In many cases reactions must be attributed to individual intolerance for the drug. Undoubtedly, when a number of patients receive arsphenamin of the same lot by the same method of administration and only one or two show reactions, it is safe to assume that they are due to an idiosyncrasy.

There are also numerous cases in which the technic of the intravenous administration is responsible for serious reactions. Schamberg, Kolmer and Raiziss [1] were the first to suggest that the cause of reactions can be attributed to impurities in the drug. "We are firmly convinced that the complex symptoms characterized by flushing, edema, etc., are due to the drug administered and not to extraneous causes."

This is the graphic formula of arsphenamin:



+ 2 Mols. H_2O or
1 Mol. CH_3OH

The analyses for arsenic, nitrogen and other elements in most of the samples correspond to the above formula with two molecules of water of crystallization. Ehrlich and Bertheim [2] thought that the compound crystallized with one molecule of methyl alcohol. Kober [3] called attention to the fact that there is no definite proof of the presence of two molecules of water of crystallization in arsphenamin. He is inclined to assume the presence of one molecule of methyl alcohol because arsphenamin usually is precipitated from solutions containing methyl alcohol.[4]

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* Read before the joint meeting of the Section on Pharmacology and Therapeutics and the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

* This work was made possible by funds accruing from the dispensing of arsphenamin.

* From the Dermatological Research Laboratories.

1. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: Experimental and Clinical Studies of the Toxicity of Dioxydiamino-Arsenobenzol Dichlorhydrate, J. Cutan Dis. **35**:286, 1917.

2. Ehrlich, P., and Bertheim, A.: Ueber das salzsaure 3, 3-Diamino-4, 4-dioxyarsenobenzol und seine nächsten Verwandten, Ber. d. deutsch. chem. Gesellsch. **45**:756, 1912.

3. Kober, P. A.: Preparation of Arsphenamin, J. A. Chem. Soc. **41**:442, 1919.

4. The authors are at present engaged in the investigation of this question.

The comparatively rapid oxidation of arsphenamin when dissolved in water or organic solvents, the difficulty of obtaining it in crystalline form and other factors make the purification of the drug practically impossible.

A compound, which cannot be repeatedly crystallized or purified by other means, is apt to contain impurities. It is possible, therefore, that the cause of the reactions observed in patients receiving intravenous injections of arsphenamin lies in the impurities of the drug.

TABLE 1.—Results of Analysis of Various Compounds of Arsphenamin Prepared in Other Research Laboratories.

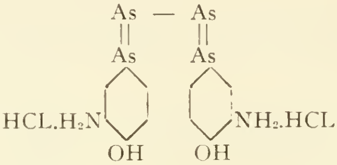
Compound	Clinical and Animal Records	Percentage of Arsenic	Percentage of Nitrogen	$\frac{As}{N}$	Deviations from Theoretical, Percentage	Mg. of Oxygen Absorbed by 100 Mg. Arsphenamin	$\frac{Mg. As}{Mg. O}$	Deviations from Theoretical, Percentage
Theoretical for arsphenamin + CH_3OH	......	31.85	5.95	5.35	...	13.47	2.34	
2551	Good	30.17	5.45	5.53	3.4	13.10	2.32	0.8
3695	Good	31.20	5.75	5.40	0.9	13.35	2.34	0.0
3695—R_6	Good	30.44	5.76	5.30	0.9	12.95	2.35	0.4
3252	Good	29.32	5.40	5.45	1.8	12.99	2.34	0.0
3735	Good	30.00	5.58	5.40	0.9	12.90	2.33	0.4
2859	Animal records unsatisfactory	30.50	5.65	5.40	0.9	12.90	2.37	1.3
3034	Animal records unsatisfactory	30.31	5.70	5.32	0.5	13.00	2.33	0.4
3181	Animal records unsatisfactory	29.30	5.45	5.37	0.5	12.80	2.30	1.7
3350	Animal records unsatisfactory	30.50	5.65	5.40	0.9	13.60	2.24	4.3
3454	Clinical records unsatisfactory	30.18	5.70	5.34	0.2	12.75	2.36	0.8
3492	Clinical records unsatisfactory	31.75	5.90	5.37	0.5	13.05	2.43	3.8
3462	Clinical records unsatisfactory	30.40	5.75	5.30	0.9	12.79	2.38	1.7

This and the following papers are devoted to the study of the chemical composition and the isolation of compounds which constitute the impurities in arsphenamin. The authors analyzed a considerable number of lots produced at the Dermatological Research Laboratories and other laboratories. The chemical composition of lots which proved to be particularly toxic for the experimental animal or produced severe reactions in patients were compared with the composition of those that were well tolerated. An attempt was made to establish a relationship between the purity of the compound and its toxicity.

This paper deals largely with arsenic and nitrogen contents and the degree of reduction of arsphenamin.

THE ARSENIC CONTENT OF ARSPHENAMIN

According to its chemical formula with either two molecules of water of crystallization or one molecule of methyl alcohol, arsphenamin contains 31.6 per cent. and 31.85 per cent. of arsenic, respectively. A lower arsenic content would indicate moisture, methyl alcohol, ether or other organic solvents as the result of insufficient drying. Inorganic impurities, such as calcium or magnesium chlorid or salts of heavy metals also lower the percentage of arsenic. Higher arsenic content, on the other hand, may result from a loss of water or methyl alcohol of crystallization, by too vigorous drying, also by the presence of impurities such as polyarsenical compounds of the following formula:



Again, higher arsenic content may indicate the presence of arsenophenols or inorganic arsenical compounds.

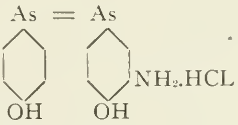
TABLE 2.—Results of Analysis of Various Compounds of Arsphenamin Prepared in Other Laboratories

Compound	Percentage of Arsenic	Percentage of Nitrogen	As / N	Deviations from Theoretical, Percentage	Mg. of Oxygen Absorbed by 100 Mg. Arsphenamin	Mg. As / Mg. O	Deviations from Theoretieal, Percentage
Theoretical for arsphenamin + CH_3OH	31.75	5.95	5.35	...	13.47	2.34	1.0
Arsphenamin from laboratory No. 3, sample A	31.44	5.74	5.51	3.0	13.20	2.38	1.7
Arsphenamin from laboratory No. 3, sample B	32.26	5.58	5.79	8.2	13.36	2.41	3.0
Arsphenamin from laboratory No. 4, sample C	31.49	5.89	5.34	0.2	13.20	2.38	1.7
Arsphenamin from laboratory No. 4, sample D	31.04	5.15	6.02	12.5	12.80	2.41	3.0
Arsphenamin from laboratory No. 5, sample E	30.87	5.14	6.00	12.5	13.05	2.36	0.8

Column 3 in Table 1 shows the percentages of arsenic in twelve lots of arsphenamin, each representing about 2,000 doses of 0.6 gm. each. Some of these values are close to the theoretical; most of them, however, are 1 per cent. lower; three preparations are 2 per cent. lower. As will be shown subsequently, it is best to consider the arsenic values in connection with nitrogen content and other data.

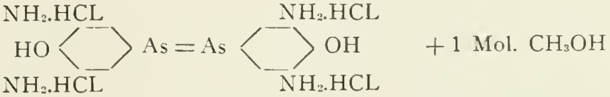
THE NITROGEN CONTENT OF ARSPHENAMIN

According to the formula, arsphenamin should contain 5.89 per cent. of nitrogen. A lower nitrogen content may be due to moisture, methyl alcohol or other organic solvents. Arsenical compounds containing no nitrogen, as for instance arsenophenol, would lower the percentage of nitrogen. Dissymmetric compounds of the following type with lower amounts of nitrogen would have the same influence:



Inorganic arsenicals or other inorganic impurities would diminish the nitrogen.

The presence of tetramino-dihydroxy-arseno benzene tetrahydrochlorid,



which contains 9.8 per cent., can account for high nitrogen in arsphenamin. This compound can easily appear as an impurity since the commercial 3-nitro-4-hydroxyphenyl arsenic acid, from which arsphenamin is prepared, frequently contains the corresponding 3-5 dinitro compound.

Column 4 in Table 1 shows that the percentage of nitrogen in normal, as well as in toxic lots, of arsphenamin is near the theoretical amount. Most of the compounds show slightly lower values, probably indicating the absence of the tetramino compound.

Ratio of Arsenic to Nitrogen.—The quantitative estimation of either arsenic or nitrogen, or both in arsphenamin, does not give one a proper idea as to its purity. In order to evaluate properly its chemical purity, we should consider the ratio between the percentage of arsenic and that of nitrogen. The theoretical percentage of arsenic in arsphenamin is 31.6, of nitrogen 5.89 per cent.; the ratio is 5.37.

To illustrate the value of the arsenic nitrogen ratio, let us consider a sample of arsphenamin which on analysis showed an arsenic content of 32.55 per cent. (0.95 per cent. higher than the theoretical content) and a nitrogen content of 5.7 per cent. (0.2 per cent. lower than the theoretical content). The ratio between these two results is 5.7, or 0.33 greater than that of pure arsphenamin. This result, therefore, may be due to the presence of an impurity containing more arsenic and less nitrogen than arsphenamin, such as the corresponding polyarsenid. This contains 50.93 per cent. arsenic and only 2.38 per cent. of nitrogen, and is more toxic than arsphenamin. The arsenic and nitrogen contents of a mixture of 95 per cent. arsphenamin and 5 per cent. of the polyarsenid would correspond to the above high ratio. Again, suppose a sample showed an arsenic content of 31.1 per cent. (0.5 per cent. lower than the theoretical content) and a nitrogen content of 6.28 per cent. (or 0.39 per cent. higher than the theoretical content). The corresponding ratio would be 4.95, or 0.42 less than that of pure arsphenamin. Such a condition may arise from the presence of an impurity containing less arsenic and more nitrogen than arsphenamin, as for example, tetramino-tetra hydroxy-arseno benzene tetra hydrochlorid, which contains 26.13 per cent. arsenic and 9.76 per cent. nitrogen. This is also more toxic than arsphenamin. The results obtained by the analysis of a mixture of 90 per cent. arsphenamin and 10 per cent. tetramino compound would give the above low ratio.

TABLE 3.—Toxicity of Various Compounds of Arsphenamin

Compound	Number of Patients	Dose Administered, Gm.	Clinical Reports, Symptoms *	Percentage of Animals That Survived Toxicity Tests†
2551	1	0.3	No reaction	100
	4	0.4	No reaction	
	3	0.6	Slight reaction	
2859	..	...	....	Did not pass the toxicity test
3034	..	...	....	Did not pass the toxicity test
3181	..	...	....	Did not pass the toxicity test
3252	3	0.6	No reaction	75
	1	0.6	Fever, chills, headache, nausea, diarrhea	
	1	0.6	Slight reaction	
3350	1	0.6	No reaction	75
	1	0.6	Severe reaction, also vomited	
3454	1	0.2	Immediate reaction	85
	1	0.4	Immediate reaction	
	3	0.3	No reaction	
	4	0.4	No reaction	
	5	0.5	No reaction	
	3	0.6	No reaction	
	4	0.4	Vomiting	
	4	0.5	Vomiting	
	5	0.6	Fever, chills, headache, nausea, diarrhea	
	21	0.6	Slight reaction	

* The clinical reports in Tables 3 and 4 were obtained from Dr. Jay F. Schamberg, Department of Dermatology of the Polyclinic Hospital, Philadelphia.

† Rats in Tables 3 and 4 received 100 mg. of arsphenamin per kilo body weight. The number of animals which survived for seven days is expressed in per cent. Six or more rats were used in each test.

Finally, let us consider an example where the arsenic content is 30 per cent. (1.6 per cent. lower than the theoretical content) and the nitrogen content is 5.6 per cent. (0.2 per cent. lower than the theoretical content). The ratio between the two is 5.36, the theoretical value. This could be due to an impurity containing neither arsenic nor nitrogen, as for example, moisture, methyl alcohol or some inorganic substance which possesses no toxic properties.

Thus we see that a valuable measure of the chemical purity of arsphenamin lies in the ratio of arsenic to nitrogen.

Examination of columns 5 and 6 in Table 1 reveals a rather remarkable agreement with the theoretical arsenic nitrogen ratio. Such compounds as No. 3034, 3492, 3462, 3695 R_6 and 3181 have the theoretical ratio; those of other compounds are very nearly so. The highest deviation from the theoretical is only 3.4 per cent. Particularly interesting is the fact that Nos. 3492 and 3462, purposely selected for this work because they were found to produce immediate reactions and other untoward symptoms in patients, show the nearest values to the theoretical. They are better than those of lots which clinically and otherwise were found good. Moreover, lots Nos. 3034 and 3181, which were definitely rejected because they did not pass the animal toxicity standards, show theoretical arsenic nitrogen ratios.

TABLE 4.—Toxicity of Various Compounds of Arsphenamin

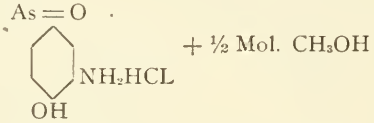
Compound	Number of Patients	Dose Administered, Gm.	Clinical Reports, Symptoms *	Percentage of Animals That Survived Toxicity Tests†
3462	1	0.6	Immediate reaction (convulsions)	100
	4	0.5	Vomiting	
	2	0.4	Vomiting	
	16	0.6	Slight reactions	
	21	0.6	No reactions	
3492	6	0.6	Vomiting	100
	6	0.6	Slight reactions	
	12	0.6	No reactions	
3695	1	0.6	No reactions	100
	1	0.6	Fever, chills, headache, nausea	
	1	0.6	Headache, nausea, vomiting	
8965–R_6	4	0.6	No reactions	100
	1	0.6	Headache, nausea, vomiting	
	1	0.6	Headache, diarrhea	
	1	0.6	Fever, headache, nausea	
3735	3	0.6	No reaction	75
	3	0.6	Slight reaction	

The values for the arsenic nitrogen ratio obtained with the arsphenamin produced at the Dermatological Research Laboratories indicate that the relationship between the arseno and amino groups is very close to that represented by its chemical formula. This fact tends to exclude the presence of such impurities as polyarsenids, tetramino, or any other compound in which the above relationship is different.

THE DEGREE OF REDUCTION OF ARSPHENAMIN ARSENIC TO OXYGEN RATIO

Arsphenamin belongs to that class of arseno compounds in which arsenic exists in the trivalent condition. Arseno compounds can be quantitatively oxidized by means of iodin solution or hydrogen peroxid, forming the corresponding aryl-arsinic acids. Arsphenamin is thus converted into 3-amino-4-hydroxyphenylarsenic acid. Gaebel[5] suggested this reaction for the quantitative estimation of arsenic since the arseno group in arsphenamin is the only one which can be oxidized in the cold by iodin. In reality, by this method one determines the amount of oxygen absorbed by the arseno group. Ehrlich and Bertheim[2] and others obtained higher results by the gravimetric method. The incompleteness of oxidation has been explained by a reversible reaction. It is possible, however, that a small part of the arsenic in arsphenamin is present in oxidized form; hence the iodin value would be slightly diminished.

When 3-nitro-4-hydroxyphenylarsenic acid, from which arsphenamin is made, is not completely reduced, or if arsphenamin is permitted to oxidize, the latter is liable to contain a quantity of 3-amino-4-hydroxyphenylarsenous oxid, which has this formula:



When the above nitro-arsenic acid is reduced too far, the corresponding arsin compound might appear as an impurity. Both the arsenous oxid and arsin are more toxic than arsphenamin. The absorption of iodin can therefore serve as a quantitative method for the determination of the degree of reduction of arsphenamin. Low iodin value would indicate insufficient reduction or the presence of arsenous oxid, while high iodin value would indicate excessive reduction or the presence of arsin. In Table 1, the iodin values are presented in terms of milligrams of oxygen absorbed by 100 mg. of arsphenamin. The theoretical amount for 100 mg. of arsphenamin is 13.47 mg. of oxygen.

In order to determine whether a certain compound is over or under reduced, it is best to establish a relationship between the arsenic content and the oxygen value, because the latter value is dependent entirely on the arsenic radical, and hence on the amount of arsenic. For instance, No. 3695 required 13.35 mg. of oxygen, while No. 3454 absorbed only 12.75 mg. If the arsenic content is disregarded, it would appear that No. 3695 is further reduced than No. 3454. But No. 3695, as shown in column 3, contains more arsenic than No. 3454 and therefore must require more oxygen. Column 8 shows the ratios between milligrams of arsenic and milligrams of oxygen absorbed by 100 mg.

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[5] Gaebel, G. Otto: Titration von Salvarsan mit Jodlösung, Arch. d. Pharm. **249**:241, 1911.

of arsphenamin. The theoretical ratio is 2.34. Column 9 shows the percentage of deviation from the theoretical. It can be seen that these ratios differ but slightly from the theoretical ratio. The largest difference is only 4.3 per cent. It is evident that almost all of the compounds are pure as far as the degree of reduction is concerned.

Compounds which did not pass the animal toxicity test or were found to cause "reactions" in patients showed as good arsenic oxygen ratio as those which fulfilled all biologic requirements. It is evident, then, that the cause of toxicity or "reactions" cannot be attributed to the presence of arsenoxid or arsin.

METHODS OF ANALYSIS

Arsenic was determined gravimetrically by digesting with a mixture of nitric and sulphuric acid and finally precipitating with magnesia mixture according to the method outlined in U. S. Public Health Bulletin.[6]

The results obtained by this method were compared with those obtained by digesting with concentrated sulphuric acid alone, precipitating with hydrogen sulphid and finally precipitating with magnesia mixture.[7]

The results obtained by both methods were in close agreement. Only duplicate checking results were considered.

Nitrogen was determined by the ordinary Kjeldahl method and was frequently corroborated by the method of Dumas for nitrogen.

The oxygen absorption was estimated from the values obtained by titrating a water solution of arsphenamin with tenth normal iodin.

SUMMARY

1. The quantitative determination of arsenic alone in arsphenamin is insufficient to estimate its purity.

2. It is suggested to establish a ratio between the amounts of arsenic and nitrogen found by analysis.

3. The degree of reduction in arsphenamin is best judged by estimating the ratio between the arsenic content and the amount of oxygen absorbed.

4. The arsenic nitrogen and arsenic oxygen ratios indicate that various samples of arsphenamin are uniformly pure.

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[6] U. S. Public Health Bull. **33**:1011, 1918.

[7] Raiziss, G. W.; Kolmer, J. A., and Gavron, J. L.: Chemotherapeutic Studies on Organic Compounds Containing Mercury and Arsenic, J. Biol. Chem. **40**:533, 1919.

5. Judged by the arsenic nitrogen and arsenic oxygen ratios, various preparations of arsphenamin rejected because of greater toxicity or severe reactions in patients appear to be as pure as those satisfactorily passing all tests.

6. The analytical study of arsphenamin leads one to believe that the impurity causing reactions in patients is present only in very small quantities.

SUMMARY OF EXPERIMENTAL STUDIES ON THE HISTOPATHOLOGIC CHANGES PRODUCED BY ARSPHENAMIN AND NEO-ARSPHENAMIN *

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In determining the toxicity or organotropism of new compounds in the course of chemotherapeutic investigations, the general custom is to administer solutions to experimental animals and arrive at conclusions on the basis of dosage in relation to the duration of life. While the results are of much value, it would appear advisable to study the less toxic and promising compounds for the kind and degree of tissue injury which they may produce in experimental animals as an additional criterion of suitableness for the treatment of disease among persons and as a guide in the preparation of new chemical compounds not only of least toxicity, but which are also least likely to produce tissue injury.

The purpose of our investigations was to study the histopathologic changes produced in rats and rabbits by the intravenous injection of single large and multiple small doses of arsphenamin and neo-arsphenamin[1] as bearing on the use of these compounds for the treatment of disease among persons and in relation to chemotherapeutic studies with new arsenical compounds prepared by one of us (Kolmer) in association with Dr. Schamberg and Dr. Raiziss.

The fatalities following the administration of arsphenamin and neo-arsphenamin in the treatment of syphilis have usually been attributed to the toxicity of the drugs and to technical errors in administration referable to the preparation of the solutions and manner of injection.

The results of studies of the gross and histologic tissue changes have usually shown the presence of some form of acute nephritis and

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* Read before the joint meeting of the Section on Pharmacology and Therapeutics and the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

* From the Dermatological Research Laboratories of Philadelphia and the McManes Laboratory of Pathology of the University of Pennsylvania.

* Investigation aided by funds accruing from the preparation of arsphenamin and neo-arsphenamin.

[1] Kolmer, J. A., and Lucke, B.: An Experimental Study of the Histopathological Changes Produced by Arsphenamin, Arch. Derm. & Syph. (in press); ibid.: An Experimental Study of the Histopathological Changes Produced by Neo-Arsphenamin, Arch. Derm. & Syph. (in press).

degenerative changes in the liver as the most prominent lesions. In Europe an acute hemorrhage meningitis has been commonly described whereas in America few or no changes in brain, cord and meninges have been found. Under these circumstances, however, but limited information can be gained regarding the tissue changes strictly ascribable to the solutions of the drugs themselves because of pathologic changes in the organs and tissues due to syphilis, for which the majority of the patients were being treated.

In our experiments rats and rabbits were injected intravenously with acid solutions of arsphenamin, that is, non-neutralized solutions in water which are extremely toxic; also with single large (0.080 to 0.100 gm. per kilo of body weight) and multiple small (0.01 mg. per kilo) doses of solutions of disodium arsphenamin prepared by adding about one-third excess of the amount of solution of sodium hydroxid required to precipitate and "clear" the solution. The single large doses corresponded to 4.8 and 6 gm. for a person of about 130 pounds. The small dose corresponded to 0.6 gm. per 130 pounds, being the maximum amount administered to persons at one time; from six to seventeen doses were administered.

Neo-arspenamin was injected into rats and rabbits in single large (0.200 gm. per kilo) and in multiple small doses (0.02 to 0.03 gm. per kilo). The former corresponded to about 12 gm. per 130 pounds and the latter to 1.2 to 1.8 per 130 pounds, from six to eighteen doses of the latter being administered.

Necropsy examinations of animals were made at varying intervals after injection, and the following organs subjected to histologic study: Cerebrum, cerebellum, brain stem and meninges, heart, lungs, liver, kidneys, suprarenals and spleen.

The histopathologic changes have varied in degree among animals receiving the same compound under identical conditions, and have generally been somewhat more severe among the rats than among the rabbits.

RESULTS OF EXPERIMENTS

The tissue injuries produced by neo-arsphenamin have generally been of the same character as those produced by arsphenamin, but, in comparison to dosage, have been less severe.

Acid or non-neutralized solutions of arsphenamin produced severe vascular injuries in all organs, characterized by congestion, hemorrhagic extravasations and the production of peculiar thrombi composed presumably of precipitates, conglutinated and hemolyzed erythrocytes. Secondary cellular degenerations and necroses followed.

Single large doses of arsphenamin and neo-arsphenamin also produced similar vascular changes of congestion, hemorrhage and thrombi of conglutinated erythrocytes in the various organs, but in a much milder degree; areas of focal necrosis and cellular degenerations in heart muscle, liver and spleen were rather prominent. The kidney lesions were composed of these vascular changes and varying degrees of tubular necrosis; the suprarenals showed well marked changes in lipoid and chromaffin contents in addition to vascular changes and cellular degenerations.

Multiple small doses of arsphenamin and neo-arsphenamin produced slight vascular changes of congestion and thrombi of conglutinated erythrocytes in the various organs; focal areas of cellular degenerations and necroses were frequently well marked, particularly in the heart and liver. The kidneys usually showed vascular and tubular changes, and the suprarenals various changes, including alterations in the lipoid and chromaffin contents.

Details regarding all of these changes observed after the administration of the different solutions of arsphenamin and neo-arsphenamin are given in the papers previously mentioned.[1]

It is to be emphasized that the maximum changes were produced by large doses of acid or non-neutralized solutions of arsphenamin, and by doses of disodium arsphenamin and neo-arsphenamin so large that they have no analogy to the amounts commonly administered to persons in one dose and at one time. While well marked tissue changes were produced by amounts of disodium arsphenamin and neo-arsphenamin comparable to the doses administered to persons in the treatment of syphilis and other infections, we do not wish to create any unfavorable impression against arsphenamin and neo-arsphenamin which have proved so valuable as therapeutic agents. *The arsphenamins and neo-arsphenamins prepared by these different laboratories produced similar changes.*

We simply wish to record the fact that neo-arsphenamin is less apt to produce these tissue injuries than arsphenamin, and to advance our knowledge of specific arsenic therapy as a means toward facilitating the more successful treatment of syphilis and other infections with arsenical compounds with the least possibility of producing tissue injury.

SOME SALIENT FACTS REGARDING THE TOXICITY OF ARSPHENAMIN AND NEO-ARSPHENAMIN *

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INTRODUCTION

The introduction of the newer arsenicals, arsphenamin and neo-arsphenamin,[1] in the treatment of syphilis brought into prominence the intravenous method of administration, formerly a less extensively used method. The intravenous method is generally considered the most effective method to use in administering these compounds, but by many it is considered more hazardous to the patient than either the subcutaneous or intramuscular methods. For these reasons, especially, the compounds should be made as free from objectionable impurities as possible; furthermore, the limitations and dangers of the intravenous method of administration should be of prime importance to syphilographers. Studies now in progress at the Hygienic Laboratory, dealing directly with the routine conduct or modifications of the official biologic tests for arsphenamin and neo-arsphenamin intended for shipment from one state to another, indicate some of the factors that may be responsible for untoward results when these drugs are administered intravenously.

OFFICIAL METHOD FOR TESTING ARSPHENAMIN AND NEO-ARSPHENAMIN

In the official method for testing arsphenamin, it is required that white rats weighing from 100 to 150 gm. shall tolerate 100 mg. per kilogram of the drug for forty-eight hours when given intravenously as a 2 per cent. alkaline solution, 0.9 c.c. of normal sodium hydroxid being used for 100 mg. of arsphenamin. White rats are required to tolerate 200 mg. per kilogram of neo-arsphenamin for seven days when given intravenously as a 4 per cent. aqueous solution. It is further required that for both compounds the rate of injection shall be 12 to 15 seconds for every 0.1 c.c. of solution.

CHEMICAL NATURE OF ARSPHENAMIN AND NEO-ARSPHENAMIN

Arsphenamin is the dihydrochlorid of 3,3′-diamino-4,4′-dihydroxy-arsenobenzene, while neo-arsphenamin is sodium 3,3′-diamino-4,4′-

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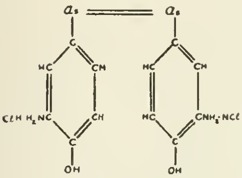
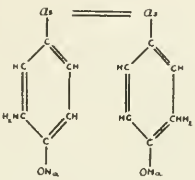
* Read before the joint meeting of the Section on Pharmacology and Therapeutics and the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

[1] These refer to the chemical equivalent of 606 and 914, formerly known exclusively as salvarsan and neosalvarsan.

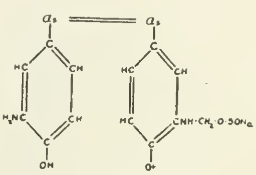
dihydroxyarsenobenzene-N-methylene sulphinate. When arsphenamin is properly made alkaline with sodium hydroxid, as is required before its administration, the disodium salt of 3,3′-diamino-4,4′-dihydroxy-arsenobenzene is formed. If oxidation occurs in any of these compounds, the more toxic substance 3-amino-4-hydroxyphenylarsenoxid may be formed. This more toxic compound is frequently referred to as "arsenoxid," and is a cleavage product in which only one arsenic atom exists in the molecule. The structures of these compounds are illustrated by the following formulae:



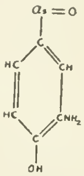
Arsphenamin.



Sodium arsphenamin.



Neo-arsphenamin.



Arsenoxid.

BEHAVIOR OF ARSPHENAMIN AND NEO-ARSPHENAMIN IN THE BODY

Neo-arsphenamin is regarded by many simply as arsphenamin in a convenient form for administration. From the formula alone it is seen that neo-arsphenamin is a modified arsphenamin and, as will be shown later, neo-arsphenamin is distinctly unlike arsphenamin as regards its behavior in the animal organism.

A statistical study of the death rate and time of death of the rats used in the official testing of arsphenamin examined during September and October, 1919, showed that a little over 80 per cent. of the animals that died within fourteen days did so within twenty-four hours, and that almost 90 per cent. of the deaths occurred within the first forty-eight hours (Chart 1). On the other hand, similar computations for neo-arsphenamin gave figures which contrasted markedly with those obtained for arsphenamin. Approximately 5 per cent. of the deaths from neo-arsphenamin occurred within the first day, 15 per cent. within the first two days, 30 per cent. within the first three days and 60 per cent. within the first four days. The highest death rate from neo-arsphenamin occurred on the fourth day. Within the fifth day the death rate was about 75 per cent. After the fifth day the death rate closely approached the curve for the death rate in "normal" animals (Chart 2).

The death rate for the entire fourteen day period is given in Table 1.

TABLE 1.—Death Rate and Time of Death in Rats After the Administration of Arsphenamin and Neo-arsphenamin

	Number of Days after Injection							
	1	2	3	4	5	6	7	8th to 14th inclusive
Rats treated with arsphenamin:								
Number of deaths	139	9	4	3	0	2	0	12
Rats treated with neo-arsphenamin:								
Number of deaths	5	10	19	37	11	6	5	19

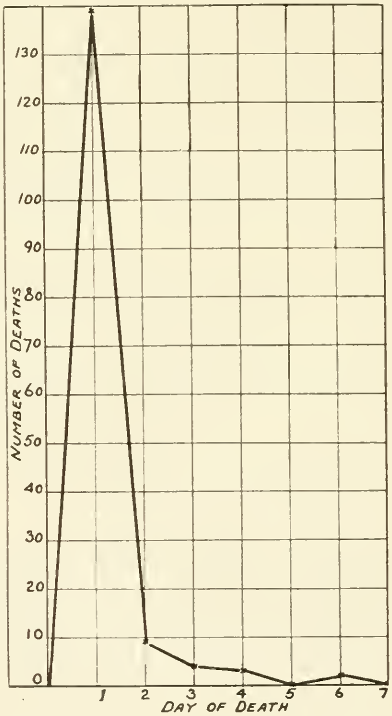


Chart 1.—Death rate and time of death of rats treated with arsphenamin.

The total number of rats injected with arsphenamin was 475, with neo-arsphenamin, 515.

Comparison of the death rate in treated and nontreated rats shows that of the 1,470 rats purchased by the laboratory from Oct. 14, 1919, to Jan. 14, 1920, only seventy-four, or about 5 per cent., of the nontreated animals died before being injected. The death rate after the second day in rats treated with arsphenamin when based on the total number of rats injected, was about 4 per cent; similarly after the seventh day in rats treated with neo-arsphenamin the death rate was about 4 per cent.

From the data given above it is evident that the two compounds behave differently in the rat, arsphenamin producing death only a short period after its administration, whereas neo-arsphenamin kills relatively slowly. An acute death after neo-arsphenamin in rats is relatively rare when tested at the official dosage, whereas after arsphenamin it is the rule. Furthermore, neo-arsphenamin rarely causes immediate symptoms in the rat, while arsphenamin usually causes rather pronounced depression when these compounds are given intravenously in the standard test doses.[2]

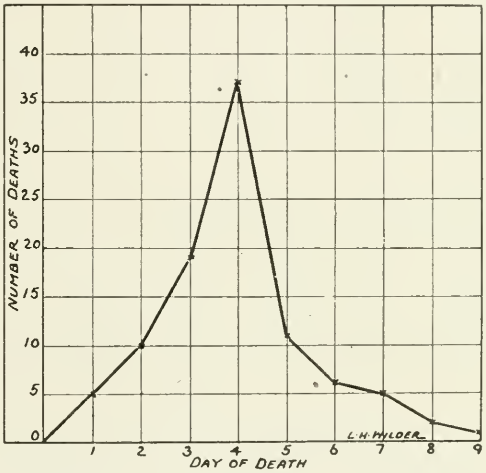


Chart 2.—Death rate and time of death of rats treated with neo-arsphenamin.

EFFECT OF CONCENTRATION OF THE SOLUTION ON THE TOXICITY OF ARSPHENAMIN

It was previously noted that the concentration of the solution of arsphenamin seemed to modify the toxicity to some extent.[3]

Quite recently Dr. G. W. McCoy, director of the Hygienic Laboratory of the United States Public Health Service[4] called attention to the fact that on investigation of the untoward results that have been reported to the Hygienic Laboratory from the use of arsphenamin made by the various American producers, it was almost invariably found that the drug had been administered in either too concentrated solution or at a too rapid rate. He therefore directed attention to these points and warned against the use of too concentrated solutions and urged that due attention should be paid to rate of administration.

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[2] Rats injected intravenously with neo-arsphenamin bleed profusely while those injected with arsphenamin bleed but little. The effects of the two compounds on the coagulation of blood in vivo, therefore, are strikingly unlike.

[3] Roth, George B.: Hygienic Lab. Bull., No. 113, July, 1918.

[4] McCoy, G. W.: The Administration of Arsphenamin. J. A. M. A. **72**:1386, 1919.

On the other hand, Nelken[5] considers that concentrated solutions given rapidly are as safe as the more dilute solutions given slowly.

Pusey[6] states that while it is true that animal experiments have shown arsphenamin to be less toxic when well diluted, the necessity for highly dilute solutions arises only when arsphenamin is contaminated by toxic substances.

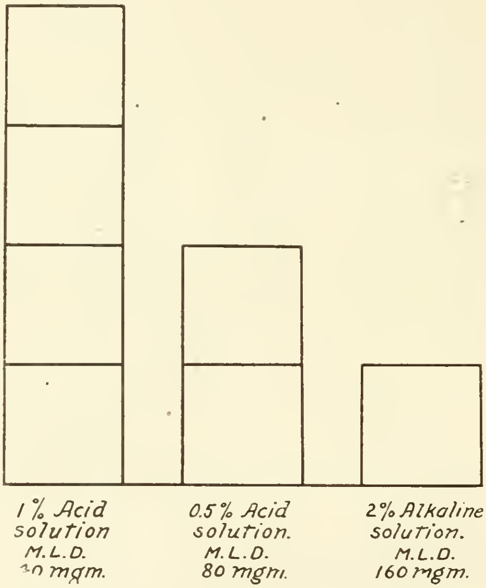

Chart 3.—Toxicity of arsphenamin before and after alkalinization.

Experiments have lately been carried out on white rats in which the official rate of administration was used, which demonstrate that the toxicity of arsphenamin under certain conditions increases as the concentration increases. The increase in toxicity is strikingly demonstrated by the more toxic acid solutions of arsphenamin. When acid solutions of arsphenamin were given intravenously to white rats, it was found that the minimal lethal dose of a high grade preparation[7] was 80 mg. per kilo when given as a 0.5 per cent. solution, and 40 mg. per kilo when administered as a 1 per cent. solution.

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[5] Nelken, A.: Administration of Arsphenamin, J. A. M. A. **72**:1695, 1919.

[6] Pusey, William Allen: Administration of Arsphenamin, J. A. M. A. **72**: 1786, 1919.

[7] This arsphenamin passed the official test at 140 mg. per kilo, the minimal lethal dose being 160 mg. per kilo

These findings not only indicate that concentration is a factor in modifying the toxicity of acid solutions, but in addition show that dilute acid solutions of arsphenamin may be given intravenously if properly administered, the above preparation in dilute acid solution having complied with the standard required for alkaline solutions of arsphenamin made by the American producers during the early period of their existence. However, it should not be inferred from this that acid solutions should be used clinically.

In this connection it is interesting to compare the toxicity of the same arsphenamin as an acid solution and as an alkaline solution. As a 2 per cent. alkaline solution the minimal lethal dose was found to be 160 mgm. per kilo, hence it is seen that as a 1 per cent. acid solution the toxicity is four times, and as a 0.5 per cent. acid solution, twice as great as a 2 per cent. alkaline solution (Chart 3).

Using a different brand of arsphenamin than the one used for determining the toxicity of acid solutions, comparative experiments were made to determine the relative toxicity of 2 and 0.5 per cent. solutions which were made alkaline with 1.06 c.c. normal sodium hydroxid per 100 mg. of arsphenamin. These solutions were administered to white rats intravenously at the same rate. The animals in each group, except in groups A and AB, received the drug alternately as a 2 and 0.5 per cent. solution. The animals in each group were from the same stock and varied but little in their weight and condition.

Except in groups A and AB, the 0.5 per cent. solution was made from the 2 per cent. solution by diluting with distilled water. The experiments appear in detail in Table 2.

TABLE 2.—TOXICITY OF ARSPHENAMIN IN WHITE RATS WHEN GIVEN INTRAVENOUSLY EITHER AS A 2 OR 0.5 PER CENT. ALKALINE AQUEOUS SOLUTION

Group	2 per Cent. Solution					Group	0.5 per Cent. Solution				
	Dose Mg.	No. Injected	No. Died in 48 Hrs.	No. Died in 14 Days	No. Lived 14 Days		Dose, Mg.	No. Injected	No. Died in 48 Hrs.	No. Died in 14 Days	No. Lived 14 Days
A	140	5	5	5	0	AB	140	5	2	2	3
B	140	5	5	5	0	B-1	140	5	3	3	2
C	140	5	3	3	2	C-1	140	5	4	4	1
D	140	5	4	5	0	D-1	140	5	3	4	1
Totals 140 mg. dose	...	20	17	18	2	....	...	20	12	13	7
Per cent.	...	..	85	90	10	....	...	..	60	65	35
E	120	5	4	4	1	E-1	120	5	5	5	0
F	120	5	1	1	4	F-1	120	5	2	2	3
G	120	5	2	3	2	G-1	120	5	0	0	5
H	120	5	0	2	3	H-1	120	5	0	0	5
Totals 120 mg. dose	...	20	7	10	10	....	...	20	7	7	13
Per cent.	...	..	35	50	50	....	...	..	35	35	65

These experiments with alkaline arsphenamin indicate that the toxicity is increased but slightly as the concentration is increased from 0.5 to 2 per cent., provided the solutions are given slowly.

INFLUENCE OF THE RATE OF INJECTION OF ARSPHENAMIN ON TOXICITY

The influence of the rate of injection of arsphenamin solutions on their toxicity was determined in guinea-pigs. The variation inherent in the animals themselves, when obtained from different sources, was eliminated by using animals obtained from the same source of supply in each series of experiments.

These experiments were carried out in two ways. In groups M and N, using guinea-pigs of practically the same weight and condition, the ten animals of each group were given 40 mg. of arsphenamin per kilo as a 2 per cent. alkaline solution intravenously; the first five received the drug rapidly, that is, in from 6 to 10 seconds, while the second five received the same solution slowly, that is, in from 95 to 128 seconds.

In groups O, P, Q and R, the 10 guinea-pigs of each group received the drug alternately rapidly and slowly; that is, animal number one received the drug rapidly, while animal number two received it slowly, and so on through the set, the dosage being 50 mg. per kilo. The summarized results are given in Table 3.

TABLE 3.—The Influence of Rate of Injection of Arsphenamin in Guinea-Pigs When Given Intravenously as a 2 Per Cent. Alkaline Aqueous Solution per Leg Vein

Group	Rapid Injection				Slow Injection			
	Number Injected	Number Died in 48 Hours	Number Died in 14 Days	Number Lived 14 Days	Number Injected	Number Died in 48 Hours	Number Died in 14 Days	Number Lived 14 Days
M	5	2	2	3	5	0	0	5
N	5	0	0	5	5	0	0	5
O	5	5	5	0	5	0	3	2
P	5	1	4	1	5	1	4	1
Q	5	5	5	0	5	0	0	5
R	5	4	4	1	5	1	3	2
Totals	30	17	20	10	30	2	10	20
Per cent.	..	57	67	33	..	7	33	67

Table 3 shows clearly that the slow injection of arsphenamin into guinea-pigs is much better tolerated than rapid injection, the mortality within forty-eight hours after rapid injection being many times greater than after slow injection. From these experiments we conclude that the rate of administration is a potent factor in modifying the toxicity of arsphenamin, the toxicity increasing as the rate is increased. Furthermore, the depression which occurs subsequent to the injection is more pronounced after rapid than after slow injection.

RELATION OF SOLUBILITY OF NEO-ARSPHENAMIN TO TOXICITY

The degree and ease of solubility of neo-arsphenamin have been found to be intimately associated with its toxicity. Preparations which were found to be incompletely soluble within 10 to 15 minutes when made up as 4 per cent. aqueous solutions, were found to kill one or more rats in every official test. In twenty-two tests which represented seventeen lots of incompletely soluble neo-arsphenamins in which 110 rats, or twenty-two sets of five each, were used, only thirty-one rats survived. In eighteen of these sets three or more animals died, in two sets two in each set died, while in the remaining two sets but one rat in each set died. The amount of insoluble matter contained in these samples was usually slight and consisted of a small amount of flocculent material which would settle in a few minutes, leaving only a film on the bottom of the mixing cylinder, while in other cases the amount was considerable. In most of these cases only the supernatant clear liquid was injected; in other cases the solutions were filtered through a soft paper filter. Filtration, however, did not cause any marked decrease in toxicity. Tests were made with two samples to determine the effect of filtration. In one sample the filtered solution killed eight of ten rats at the official dose, while the unfiltered solution killed all of ten rats injected in the same manner. In the second sample the result was practically the same as the preceding.

All of these preparations were reported by the manufacturer to be readily soluble in his tests so that the decrease in solubility mentioned above probably occurred after the products left the factory. As it cannot be definitely stated whether these preparations would have passed the official toxicity tests conducted by the Hygienic Laboratory before the preparations became less soluble, positive conclusions are unwarranted from the above findings. In the manufacturers' tests, however, all of these preparations were of satisfactory toxicity.

From these observations we have come to regard incompletely or slowly soluble products as dangerous, even if filtered. The marked toxicity noted above may have been due either to an increase in the amount of shaking of the solution or to the physical state of the product itself. The latter explanation seems the more probable as the amount of shaking in the above experiments was no more than was done when completely soluble preparations of satisfactory toxicity were examined.

THE EFFECT ON TOXICITY OF SHAKING A SOLUTION OF NEO-ARSPHENAMIN OR ARSPHENAMIN IN THE PRESENCE OF AIR

Neo-arsphenamin.—When neo-arsphenamin is dissolved in freshly glass distilled water as a 4 per cent. solution and shaken vigorously[8] by hand with about twice its volume of air, it rapidly increases in toxicity, presumably from the formation of "arsenoxid." In most of the tests a domestic neo-arsphenamin (P — 4) was used to determine the effect of shaking. This preparation was an unusually high grade preparation passing the official tests at 420 and failing at 500 mg. per kilogram of rat. When this preparation was made up as a 4 per cent. aqueous solution and shaken vigorously by hand in a glass-stoppered 25 c.c. cylinder at room temperature (about 20 degrees C.), its toxicity was over four times as great as that of the unshaken solution. When shaken for 5 minutes, it failed to pass at the official dosage of 200 mgm. and when shaken for 1 minute it failed to pass at a dosage of 300 mg. and gave only a 60 per cent. pass at both 200 mg. and 140 mg. dosages.

Vigorous shaking for one minute in the presence of air will therefore increase the toxicity of high grade neo-arsphenamin considerably and thereby render it a dangerous borderline product. There was no color change in this product (P — 4) even after shaking for 10 minutes in the manner described above.

By using a lower grade domestic neo-arsphenamin (B — 4), it was found that vigorous shaking for one minute in the presence of air resulted in a complete failure when tested at the standard test dose of 200 mg. When tested in the official manner as an unshaken solution, this preparation passed at 200 mg., but failed at 240 mg. per kilogram. It was unlike P — 4 in that a slight deepening of the light canary yellow solution to a deep golden yellow occurred after shaking for ten minutes. However, after shaking for one minute no color change was detected in this preparation (B — 4).

Arsphenamin. — The effect on toxicity of shaking a solution of arsphenamin was determined by using an alkaline solution of arsphenamin, the amount of alkali added being a trifle greater than was required to form the disodium salt, that is, 1 c.c. of normal sodium hydroxid was added for every 100 mg. of arsphenamin.

For these experiments a domestic arsphenamin (B — 2) was used. This lot passed the official tests at 140 and failed at 160 mg. per kilo (see Table 4).

After making a 2 per cent. aqueous alkaline solution of disodium arsphenamin as described above, it was shaken vigorously in a 25 c.c.

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[8] Approximately 230 excursions per minute.

glass-stoppered cylinder at room temperature in the presence of about twice its volume of air for a period of ten minutes. When tested on rats in the official manner, eight of ten rats died at a dosage of 100 mg. per kilo, while only two of ten rats died when given a similar dose of the unshaken solution.

The symptoms after the administration of the shaken solution were especially severe, the animals developing marked dyspnea and extreme weakness immediately after the injection. These symptoms lasted for about an hour. The control animals which received the unshaken solution became slightly drowsy, but were able to walk immediately after the injection.

These experiments conclusively show that the toxicity of a solution of arsphenamin as prepared for administration to man is materially increased by shaking for ten minutes in the presence of air, and that vigorous shaking should be avoided after the alkali is added. Unlike neo-arsphenamin, the solution was distinctly darkened after shaking for several minutes, and decidedly darkened after shaking for ten minutes.

COMPARISON OF THE TOXICITY OF ARSPHENAMINS AND NEO-ARSPHENAMINS MADE IN THE UNITED STATES WITH THOSE OF FOREIGN MANUFACTURE

It is generally recognized that the standards set by the Hygienic Laboratory for the purity of arsphenamin and neo-arsphenamin are sufficiently rigid to insure products of high quality. In order to ascertain whether United States products compared favorably with foreign products a toxicologic study was made of five arsphenamin and five neo-arsphenamin preparations made in the United States, also

TABLE 4.—COMPARATIVE TOXICITY OF ARSPHENAMIN AND NEO-ARSPHENAMIN PREPARATIONS MADE IN THE UNITED STATES WITH THOSE OF FOREIGN MANUFACTURE

Sample of Arsphenamin	Maximal Tolerated Dose, Mg. per Kilo.	Minimal Lethal Dose, Mg. per Kilo.	Arsenic Content, per Cent.	Sample of Neo-Arsphenamin	Maximal Tolerated Dose, Mg. per Kilo.	Minimal Lethal Dose, Mg. per Kilo.	Arsenic Content, per Cent.
U. S. Products:				U. S. Products:			
B-1	100	120	31.3	B-3	200	240	19.0
B-2	140	160	29.8	B-4	200	240	18 4
P-1	180	220	31.3	P-3	280	320	18.8
P-2	120	140	30.5	P-4	420	500	19.5
C-1	160	180	31.5	C-2	240	280	18.6
Foreign Products:				Foreign Products:			
German H-1	80	100	32.1	German H-4	260	300	19.7
German H-2	120	140	32.0	German H-5	240	300	18.8
German H-3	60	80	31.0	French B-1	240	280	19.5
French S-1	60	80	30.0	French S-2	120	150	19.8
Canadian M-1	80	100	24.9	Canadian T-1	200	240	18.8
Japanese T-1	140	160	31.8	Japanese T-2	360+	?	17.7

of six arsphenamin and six neo-arsphenamin preparations of foreign manufacture. These preparations were all administered intravenously to white rats in the official manner, the minimal lethal dose for arsphenamin being the minimal dose which killed 60 per cent. or more of the animals within forty-eight hours, whereas for neo-arsphenamin the minimal lethal dose refers to the minimal dose which killed 60 per cent. or more of the animals within seven days. The results of this study are summarized in Table 4.

It may be concluded from this study that the arsphenamins made in the United States are generally less toxic than those of foreign manufacture, while the domestic neo-arsphenamins compare favorably with the foreign neo-arsphenamins examined and in certain instances are decidedly less toxic than most of the foreign products.

CONCLUSIONS

The results of the foregoing experiments warrant the following conclusions:

1. Neo-arsphenamin behaves differently in the animal organism from arsphenamin and should not be regarded simply as arsphenamin in a convenient form for administration.

2. When administered intravenously and at a constant rate, acid solutions of arsphenamin are much more toxic than the corresponding alkaline solutions, the toxicity of the acid solutions increasing with the concentration.

3. A properly alkalinized 2 per cent. arsphenamin solution when administered intravenously and in high dosage is slightly more toxic than a 0.5 per cent. solution.

4. The toxicity of properly alkalinized arsphenamin increases greatly as the rate of its intravenous administration is increased. Rate of administration is, therefore, an important factor in determining toxicity.

5. When neo-arsphenamin is found to dissolve with comparative difficulty, it is generally highly toxic and should be discarded.

6. Shaking aqueous solutions of neo-arsphenamin or alkalinized arsphenamin in the presence of air increases their toxicity markedly. When a 4 per cent. solution of neo-arsphenamin is shaken vigorously for ten minutes its toxicity is more than quadrupled.

7. Arsphenamin preparations made in the United States are generally less toxic than those of foreign manufacture.

8. Neo-arsphenamin preparations made in the United States compare favorably, and in certain instances are decidedly less toxic than most of the foreign products.

THE APPLICATIONS AND LIMITATIONS OF THE ARSPHENAMINS IN THERAPEUTICS *

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Ten years have now elapsed since Ehrlich announced the synthesis of arsphenamin and expressed his hopes for its therapeutic efficacy in syphilis in man based on its effect on the disease in the rabbit. The failure of the simple, experimentally determined rationale of the single dose cure, when applied to man, abruptly precipitated the use of the drug on a period of quasi-empiricism from which we are now slowly emerging. In fact, many valuable empiric rules of thumb which have marked our progress along the way of rationalization still survive. The one great solvent of therapeutic perplexities, time, has not yet had its full say on the ultimate values of the arsphenamin in syphilis. In frambesia, relapsing fever, rat-bite fever, and other less resistant spirilloses, the question is perhaps settled. But until a generation of syphilitic humanity, treated with arsphenamin, has been born, studied, died and passed through a gross and microscopic necropsy examination whose searching quality we are only beginning to appreciate, the full applications and limitations of the arsphenamins in the therapeusis of the disease are open to discussion.

Within the last few years the experimental and analytic basis for a new rationale of arsphenamin therapy has developed rapidly. Among notable contributions one recalls the basic work of Warthin [1] on the pathology of the disease; Noguchi and Akatsu,[2] Nichols [3] and

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* This discussion is based on material collected from a series of 30,000 intravenous injections of arsphenamin under hospital conditions. Where the term "injection" is used without modification in connection with arsphenamin, intravenous injection should be understood.

* Read before the joint meeting of the Section on Pharmacology and Therapeutics and the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

[1] Warthin, A. S.: The New Pathology of Syphilis, Am. J. Syph. **2**:425, 1918; The Persistence of Active Lesions and Spirochetes in the Tissues of Clinically Inactive or "Cured" Syphilis, Am. J. M. Sc. **152**:508, 1916.

[2] Noguchi, H., and Akatsu, S.: Immunological Studies on pure Cultures of Various Spirochetes, J. Exper. Med. **25**:765, 1917.

[3] Nichols, H. J.: Observations on the Pathology of Syphilis, J. A. M. A. **62**:466 (Aug. 8) 1914.

Reasoner [4] on spirochetal strains, the investigations of Akatsu and Noguchi [5] on the arsenical and mercurial tolerance of spirochetes; the studies of Danysz,[6] Rieger,[7] Schamberg [8] and his collaborators on the biochemistry and toxicology of the arsphenamins, and the work of Friedberger and Masuda, Weisburg, Bachucke, Toyama and Kolmer [9] on the nonspecific formation of agglutinins, hemolysins and other antibody-like substances, under the influence of the drug. From one or another phase of this work have sprung various efforts of syphilographers of experience [10] to apply to therapeutics the principles suggested by laboratory research, as in the intensive technic proposed by Pollitzer,[11] and the utilization of antibody effects in the intraspinous technic of Swift and Ellis.[12] These rationalizations are not made any less commendable in intent by the fact that cures, as determined by reinfection, may be the sequels of the most irrational and haphazard procedures. Contemplation of the reinfection field in the literature is the best antidote for the conception that there is a standard arsphenamin treatment for the cure of a resistant spirillosis such as syphilis. Almost anything will cure some patients, almost nothing avails in others. A discussion of arsphenamin therapy must therefore take cognizance to a high degree of the fact that the drug is only one factor in a complex, and that what it accomplishes in one case may be no guide to its efficacy in another. It is merely one of the factors in the

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4. Reasoner, M. A.: Some Phases of Experimental Syphilis with Special Reference to the Question of Strains, J. A. M. A. **67**:1799 (Dec. 16) 1916; Early Death from Cerebral Syphilis, with Successful Rabbit Inoculation, J. A. M. A. **66**:1917 (June 17) 1916.

5. Akatsu, S., and Noguchi, H.: The Drug-Fastness of Spirochetes to Arsenic, Mercurial and Iodid Compounds in Vitro, J. Exper. Med. **25**:349, 1917.

6. Danysz, J.: Les propriétés physicochémiques des produits du groupe des arsénobenzenes, leurs transformations dans l'organisme, Ann. d. l'Inst. Pasteur **31**:114, 1917.

7. Rieger, J. B.: Notes on the Decomposition of Arsphenamin, J. Lab. & Clin. Med. **4**:181, 1918.

8. Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: Experimental and Clinical Studies of the Toxicity of Dioxydiamino-Arsenobenzol Dichlorhydrate, J. Cutan Dis. **35**:286, 1917.

9. Toyama, I., and Kolmer, J. A.: The Influence of Arsphenamin and Mercuric Chlorid on Complement and Antibody Production, J. Immunol. **3**:301, 1918. (This article is particularly valuable.)

10. Schreiber, E.: Ueber die Wirkungsweise des Salvarsans und Quecksilbers bei der Syphilis, München. med. Wchnschr. **61**:522, 1914.

11. Pollitzer, S.: The Principles of the Treatment of Syphilis, J. Cutan. Dis. **34**:633, 1916.

12. Swift, H. F., and Ellis, A. W.: The Treatment of Syphilitic Affections of the Central Nervous System with Special Reference to the Use of Intraspinous Injections, Arch. Int. Med. **12**:331, 1913. Swift, F.: A Study of Serum Salvarsanized in Vitro, J. Exper. Med. **24**:373, 1916.

course of the disease. The specificity and mathematical exactness of its effects in given dosages, of which Ehrlich dreamed, has gone glimmering among the pitfalls of spirochetal individuality and variations in human susceptibility. No amount of the drug by any technic of administration can avail, it would seem, in the face of a combination of a given low specific tissue resistance in the patient, and a high selective tendency to localize in the same tissue on the part of the infecting organism. A susceptible nervous system and a neurotropic spirochete probably explain some of the most conspicuous failures of arsphenamin. To work out the possibilities of the arsphenamin factor in the outcome of any disease in its relation to the potentialities of the infecting organism and the resistance of the patient is the ultimate problem of arsphenamin therapeusis.

TWO METHODS OF ADMINISTRATION OF ARSPHENAMIN

Broadly speaking, two types of therapeutic employment of the arsphenamins are recognizable. While the two overlap to some extent and each contains some elements of the other, an appreciation of their respective merits and defects contributes much to the rationalizing of arsphenamin procedure. Massive or intensive technic aims primarily at spirocheticidal effects and sacrifices the immunizing or resistance-building powers of the drug. Such a technic calls for the highest possible concentration of the drug in the blood and tissues, maintained for the longest possible time which the patient's tolerance will permit. The methods employed for this purpose vary from the administration of small daily doses of a decigram or two for a number of days, to the administration of maximum doses for two or three days in succession, followed by a rest period or a change to some other mode of treatment. Such methods, I believe, involve an increased risk of cumulative toxic effects and of failure as expressed in the occurrence of neurosyphilitic accidents, which must be compensated for by a demonstrated superiority in the form of a high percentage of cures. I do not think there exists conclusive evidence demonstrating such a superiority. For this reason, I feel that the safer plan for the average case is a combination of massive and immunizing technic.

The logical field for massive technic is the stage of the disease in which the infecting organism is accessible both in blood stream and tissues, where it can feel the full force of the direct spirillicidal action. In the later stages, when the organism is walled off by the infiltrations and fibroses so distinctive of the pathology of syphilis, and protected from the action of blood-borne therapeutic agents by endarteritic occlusion of the blood supply, it seems to me that the hope of radical spirillicidal action is illusory and not to be depended on. In its place we must substitute a stimulation of the native or intrinsic protective mechanism of every tissue of the body. In syphilis at least, I question whether this mechanism has the high degree of specificity so often credited to it. It is perhaps proteolytic and bacteriolytic rather than purely spirocheticidal. If we are to employ a drug such as arsphenamin at such a stage, we should, it seems to me, employ it by a technic which brings out more of its immunity-stimulating power, even though it may be at a sacrifice of some of its direct spirillicidal action. That the sacrifice of its direct spirillicidal action is not as complete in less massive technics than some observers seem to believe, is suggested by the work of Katz,[13] for example, who found that half the maximum dose seemed to destroy surface spirochetes as promptly and effectively as the larger doses.[14]

My conception of the immunization technic of arsphenamin administration [15] is that of graduated, moderate dosage at safe intervals for long periods, with rest intervals designed to prevent the arsenic fastness described by Akatsu and Noguchi.[5] Moderate dosage means one-half, increasing to two-thirds, the Ehrlich maximum. A safe interval is one week. An average series or period is from six to eight injections. An average rest interval between series is from four to twelve weeks. An average number of such series is three or four.

From these two types of technic, a wide variety of combinations may be made, suited to the taste and temperament of the therapist, to his conceptions of the immunology of syphilis, to the stage of the infection, to the nature of the complications, and to the tolerance of the patient. The immunization extremist should, it seems to me, employ intramuscular administration because of the slow absorption and prolonged action thus obtained. Immunization technic, as ordinarily used in intravenous injection, enters into and explains some of the effectiveness of intraspinous therapy, of which it forms the intravenous part. It explains the nonspecific and indirect action of arsphenamin on conditions such as tuberculosis, blastomycosis, anthrax and trichinosis, in which no direct parasiticidal action is likely. Modifications of it are, to my mind, the methods best adapted to the fully entrenched and late syphilitic infection.

On the other hand, the efficiency of the spirillicidal technic in early cases is so far demonstrated that it must be given a place in general syphilotherapy proportional to the earliness of the infection. In primary syphilis and in the florid eruptive stage, a massive or spirillicidal arsphenamin therapy is imperative. My personal concession to it consists of the administration of three almost maximum doses in the first nine days. To one who plans to rely entirely on a spirillicide technic, this is not intensive enough. Pollitzer's [1] three doses in three days, and Schamberg's [16] 3 dg. doses on alternate days are familiar and usually effective if properly guarded with mercury. On the other hand, I feel that no massive technic is as yet a substitute for immunity building, and I accordingly follow my single massive attack by weekly injections to the total number of eight or nine, before beginning the first arsphenamin rest interval. In early infections this should not be more than from four to six weeks, as pointed out by Gennerich, and should be protected by mercury as in shorter course technics.

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[13] Katz, T.: Ueber intravenöse Injektionen von konzentrietem Neosalvarsan, München. med. Wchnschr. **60**:2337, 1913.

[14] If for no other reason, the use of arsphenamin in syphilis should be obligatory as the only existing means of sterilizing the patient in the interest of the public health.

[15] Toyama, I., and Kolmer, J. A.: The Influence of Arsphenamin and Mercuric Chlorid on Complement and Antibody Production, J. Immunol. **3**:301, 1918. (This article summarizes the experimental basis of this technic.)

COMBINATION OF MERCURY WITH ARSPHENAMIN IN SYPHILIS

The phrase "protected with mercury," discloses the cardinal weakness of the arsphenamin therapy of syphilis. The tendency to substitute arsphenamin for mercury is the blunder of the inexpert syphilotherapist. The point to be remembered is that the more massive and the shorter the arsphenamin phase is made, the less immunity or resistance is secured. Patients who have experienced nothing but the spirillicidal action of arsphenamin at the hands of an unbalanced enthusiast, are exposed to the gravest accidents, bereft as they are of physiologic defense.[18] The deficiency is to be made up to some extent by more arsphenamin. From the appreciation of this fact arose the Ehrlich aphorism "the remedy for neurorecurrence due to arsphenamin is more arsphenamin." Why more arsphenamin? Not as I conceive it, for its spirillidical effect alone, so much as for its immunity and defense stimulating qualities, brought out by the longer, more moderate dosage course.

There exists, however, ready to hand, another and even more important means than "more arsphenamin" for reinforcing the transient resistance and immunity developed by this drug. Mercury is the natural complement of a spirillicidal agent in syphilis.[19] The injunction to use it in effective form should appear on the label of every ampule of arsphenamin. In contrast to arsphenamin as a direct spirillicide in the human body, the failure of mercury has been demonstrated from a variety of angles.[20] But as an immunity stimulator it is sovereign. It must be so used in conjunction with every type of arsphenamin administration, that it fills in the gaps between the action of its more spectacular confrère with solid substantial resistance. Why not rely on it entirely? Because its action is slow when speed is most needed, and its toxicity is high, especially in prolonged administration. Arsphenamin is the broom that sweeps, mercury is the club that crushes. More than once one is impelled to wonder whether overmassive mercurialization does not wreck the patient as it "cures" the disease. Arsphenamin, on the other hand, discriminatingly employed, has a tonic action that is an inexpressible relief from the depressant action of mercury.

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[16] Schamberg, J. F.: A Second Attack of Syphilis Two Years After the First; Curability of the Disease, J. A. M. A. **73**:826 (Sept. 13) 1919.

[17] Gennerich: Die bisherigen Erfolge der Salvarsanbehandlung im Marinelazarett Wik, München. med. Wchnschr. **61**:513, 1914.

[18] Gennerich (Footnote 17) was one of the first to call attention to this aspect of the therapy. See also Pusey, W. A.: The Present Situation in Syphilis, Am. J. M. Sc. **146**:497, 1913. Compare also Toyama and Kolmer (Footnote 15) on the inhibitory effect of large doses on agglutinin formation.

[19] Compare Schreiber, Footnote 10, who discusses the complementary action of the two drugs.

To secure the maximum combination of benefits, with the minimum of defects from both drugs, I believe it is essential, especially in early cases, to use them simultaneously rather than alternately. Prolonged observation of the effect of this combination has made me believe them actually synergistic in effect, and without permanent damaging effect on the excretory mechanism.[21] By simultaneous use, the slowly developed mercurial immunity overlaps the deficiencies of the transitory arsphenamin immunity, and fills the gaps between the peaks of the latter's spirillicidal efficiency. I ought to say, however, that I frankly disapprove of the routine use of insoluble mercurials such as the salicylate, gray oil, etc., in simultaneous combination with arsphenamin.[22] The leaving of mercurial depots of unknown capacity in the tissues of patients of unknown resistance and tolerance[23] in the early months of a course of treatment which may last Heaven only knows how long, is an adventure in speculative therapy that my experience with the kidney in syphilis will not countenance. The 4 gm., 30 to 50 per cent. inunction and the soluble mercurial salt, as simultaneous and interim treatment, have for the past three years accomplished all I could desire of mercury in the treatment of syphilis.[24]

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[20] Lomholt, S.: Die Zirkulation des Quecksilbers im Organismus, Arch. f. Dermat. u. Syph. **126**:1, 1918. This is an important monograph with a bibliography of 339 titles. For a discussion of the opposing views espoused by Neisser and Finger see page 65. See also Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: The Chemotherapy of Mercurial Compounds, Am. J. Syph. **1**:1, 1917. Lomholt, S., and Kissmeyer: Zur Wirkung des Quecksilbers auf Syphilis, München. med. Wchnschr. **64**:1292, 1917.

[21] For the opposing view, see Loewy, A., and Wechselmann, W.: Experimentelle Untersuchungen über die Wirkung intravenöser Salvarsaninjektionen auf die Funktion der Niere insbesondere bei bestehender Quecksilberintoxikation, Berl. klin. Wchnschr. **39**:1342, 1913.

[22] Pollitzer, Footnote 1, as an example of alternate use of two drugs.

[23] For an analysis of this factor in the use of insoluble salts, see Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: A Study of the Comparative Toxicity of the Various Preparations of Mercury, with a Histological Study of Experimental Mercurial Nephritis, J. Cutan. Dis. **33**:819, 1915.

You will see from my high estimate of the value of prolonged maintenance of resistance in syphilis, that I have little faith in the shortened or abortive procedures which have had such vogue in cases seen in the earlier weeks or months of the infection. In the present dubious state of knowledge as to the immunity mechanism of reinfection, superinfection and so-called clinical cure, I feel that it is inexcusable to give less than from eighteen to twenty-four arsphenamin injections in an early case. These I mass into the first year, employing the spirocheticidal opening attack of three injections in nine days, as part of the first course of eight injections and from four to six weeks intervals between the later courses of six. Mucous recurrences, a test of the effectiveness of an average technic, and not uncommon after twelve unsystematic and scattered injections, have thus far never developed in my experience, in such a course, with its accompanying 300 inunctions. With inunctions given in courses of forty and eighty, and with rest intervals of one and two months overlapped by arsphenamin, it will be apparent that mercurialization extends a considerable period beyond the cessation of the arsphenamin phase.

USE OF ARSPHENAMIN IN LATE SYPHILIS

In the therapy of established or late syphilis, to my mind, the spirillicidal action of arsphenamin, while still important, and maintainable to a marked degree by reasonable dosage and interval, is no longer the paramount goal of the use of the drug. New factors enter into the case, calling for increasing individualization and greater conservatism in the assumption of treatment risks. The prospect of radical extirpation of every spirochete diminishes to the point where we must realize that the arsphenamin miracle has the odds against it. Knowledge of when to stop and observe often comes to be worth more than the rash or over-enthusiastic impulse to go ahead. In late and intrenched infections, therefore, I tend even in the absence of gross contraindications, to be more leisurely in my attack, and to extend the same course of treatment used in early infections, over a longer period, especially by increasing the interim mercurialization periods between arsphenamin

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24. Hoffmann, E.: Ueber eine nach innen gerichtete Schutzfunktion der Haut (Esophylaxie) nebst Bemerkungen über die Entstehung der Paralyse, Deutsch. med. Wchnschr. **45**:1233, 1919. This author explains part of the effectiveness of inunctions by an arousing of the protective functions of the skin. See also Stokes, J. H.: Observations on the Intensive Combined Treatment of Syphilis, Mississippi Valley M. J. **25**:11, 1918. Schamberg, Footnote 16.

courses. Thus the average late interval is from four to six months between arsphenamin series, instead of the corresponding number of weeks, and the tonic action of the arsphenamin is distributed throughout the mercurialization phase, instead of being sacrificed to spirillicidal action by being massed ahead of it, as in early infections. At the same time, a decided measure of spirillicidal effect in the late infection is conserved by the massing of the groups of arsphenamin injections into compact units, insteads of scattering them by long intervals between individual injections.

In the early months of a syphilitic infection, occurring as it usually does in a young person in good general health, treatment risks are more safely taken, and routine therapeutic hammering better tolerated than in the late manifestations of the disease, when the damage done by the infection combined with the handicaps of age and the pressure of living, make the late syphilitic a less eligible subject. The therapy of late syphilis must therefore strike a balance between the gravity of the disease process and the physical handicaps of the patient. The gravity of the process must be determined by searching examination of those parts of the body whose functional integrity is necessary to life. For example, it is one of the sins of the symptomatic outlook on the disease, that a therapist, seeing the cutaneous syphilid, and knowing the ready response of such lesions to arsphenamin, administers a liberal dose of the drug, only to throw his patient into almost a cardiac fatality through his failure to consider the structural involvement of the heart, an organ necessary to life. It is equally possible to watch with enthusiasm the rapid response of an osseous lesion and to discharge the patient when it has disappeared, or to put him on minor therapy, while a neurosyphilis in the same patient, overlooked through inadequate examination, goes merrily on to an ultimately crippling and fatal outcome. Arsphenamin is capable of doing immense harm when its employment is intrusted to the spectacularly-minded, whose appreciation of its astonishing symptomatic effects blinds them to its transient action and its weaknesses. It is worth while, too, in these cases, to discourage the over-sanguine frame of mind that a limited experience with the arsphenamins is apt to develop. Remarkable as its effects undoubtedly are, it cannot restore cor bovinum, or the bulged aorta to normal, nor bring back vision to the sightless eyes in advanced simple primary optic atrophy. As an essential preliminary to all use of arsphenamin therapy in late syphilis, then, as a guide both to intensity and prognosis, I would place the complete and careful clinical and serologic examination of the entire body. Without the knowledge which such an examination gives, one proceeds about his use of the drug with only half vision if not outright blindness.

AXIOMS GOVERNING SUCCESSFUL USE OF ARSPHENAMIN

Every user of arsphenamin in large amounts ultimately develops a group of axioms, epitomizing its applicability, limitations and contra-indications for his own experience. The most servicable of these are, to my mind:

The arsphenamins are the drugs of election where there is marked renal damage, and in acute syphilitic nephritis.[25] Schamberg and his collaborators [26] have estimated its toxicity for the kidney as one fiftieth that of mercury, for example.

The liver metabolizes arsphenamin and stores arsenic.[27] Watch it therefore, to forestall accidents, and when it is structurally damaged, reduce dosage and expect lowered general tolerance of the drug.

The arsphenamins are distinctly vasculotoxic.[28] Such effects are particularly serious in vascular syphilis of the brain and in the damaged myocardium,[29] and compel a greater dependence on mercury. The vasculotoxic effect seems especially marked in acute processes, and probably blends with the Herxheimer reaction.

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[25] Hoffmann, E.: Ueber akute syphilitische Nierenentzündung in der Frühperiode (Nephritis syphilitica acuta praecox), Deutsch. med. Wchnschr. **39**:353, 1913. Stokes, J. H.: Acute Syphilitic Nephritis from the Standpoint of Diagnosis and Salvarsan Treatment, with Report of a Case. J. A. M. A. **66**: 1191 (April 15) 1916. Cole, H. N.: Acute Syphilis of the Kidney, Report of a Case, Am. J. Syphilis **4**:46, 1920.

[26] Schamberg, Kolmer and Raiziss, Footnote 23.

[27] Riebes, E.: Ueber die Verarbeitung des Salvarsans und Neosalvarsans im Organismus, Arch. f. Dermat. u. Syph. **118**:757, 1913. Stühmer, A.: Zur Topographie des Salvarsans und Neosalvarsans, Arch. f. Dermat. u. Syph. **120**: 589, 1914. The following articles voice an interesting controversy over the significance of jaundice in arsphenamin treatment. Milian, G.: Trois cas d'ictère au cours du traitement à l'arsenobenzol, leur nature syphilitique, Bull. et mém. Soc. méd. de hôp. de Paris **43**:821, 1919; abstr., J. A. M. A. **73**:1858 (Dec. 13) 1919. Deux cas d'ictère au cours du traitement par le néo-salvarsan, Paris méd. **7**:191, 1917. Sicard, Haguenau and Kudelski: Traitement de la syphilis nerveuse chronique, les éléments de contrôle de la médication novarsénicale, Bull. et mém Soc. méd. d. hôp. de Paris **43**:833, 1919.

[28] Caesar, V.: Sieben Fälle von cerebralen Erkrankungen nach Salvarsanbehandlung, Dermat. Ztschr. **20**:569, 1913; abstr., J. Cutan. Dis. **32**:526, 1914. Labbé, M., and Langlois, S.: Purpura hémorragique aigu par intoxication arsénicale, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:786, 1919; abstr., J. A. M. A. **73**:1645 (Nov. 22) 1919. Pearce, L., and Brown, W. H.: Chemopathological Studies with Compounds of Arsenic. II. Histological Changes in Arsenic Kidneys, J. Exper. Med. **22**:525, 1915. The antagonistic effect of adrenalin on the vasoparetic action of arsphenamin was originally urged by Milian as explaining the efficiency of the former in hemorrhagic encephalitis due to arsphenamin. For a more recent statement of his views see: Milian, G.: (Administration of Epinephrin), Paris méd. **8**:81, 1918; abstr., J. A. M. A. **70**:1041, 1918. For recent work on the effect of arsphenamin on the adrenal, see: Hirano, N.: Experimental Studies on the Investigation of the Nature of Anaphylactoid Reactions Caused by Repeated Intravenous Injection of Salvarsan, Kitasato Arch. Exper. Med. **3**:1, 1919; abstr., J. A. M. A. **72**:1947, 1919.

Arsphenamin, when first administered, produces a flare-up of a syphilitic process which is proportional to the acuteness of the process and the size of the dose administered. This so-called Jarisch-Herxheimer reaction, familiar enough in the eruptive period, occurs at every stage and with varying intensity in every structure affected by syphilis. If a large dose is given in the presence of a sluggish process, or a small dose in an acute process, there will be a focal response which is of some assistance in diagnosis. On the other hand, if a large dose is given in an active process, the seriousness of the outcome will be proportional to the importance of the involved structures. Thus a manifestation intrinsically no more serious than a gummatous ulceration of the larynx may be responsible for death by asphyxiation through edema caused by a Herxheimer reaction from overdosage in an active though late process. The estimation of the acuteness or activity of a syphilitic process and the importance of the structures involved thus constitutes an important factor in determining the advisability of using arsphenamin with or without preparation, and in moderate or large dosage. Mercury, because of its slower action, should be a preliminary to the use of arsphenamin in all first courses of treatment when important structures are involved. The more acutely the nervous system in particular is affected, the longer should the mercurial preparation be. As a mercurial for preparation purposes, I prefer a soluble salt, unless there are renal contraindications or cardiac decompensation, in which case the slower inunction is desirable.

The tolerance of the arsphenamins is diminished in varying but pronounced degrees by factors which have likewise a pronounced influence in increasing the gravity of a syphilitic infection. Among these I include foci of septic infection, even if latent, which increase the susceptibility of the skin to exfoliative accidents and reduce the resistance of the kidney to therapy.[30] Acute respiratory infections and influenza are apt to be exaggerated into pneumonia by arsphenamin administration.[31] Febrile conditions complicating syphilis, especially pulmonary tuberculosis which is on the down grade, usually responds unfavorably, in my experience.[32] On the other hand, if the patient's resistance is good, the response may be gratifying. Pyelonephritis and severe cystitis may sharply diminish the tolerance of arsphenamin and lead to violent febrile reactions. Urinary retention from neurogenous atonic bladders and enlarged prostates has a definite effect in retarding the progress of patients under treatment. I consider it a matter of great importance to secure a careful history of previous dermatoses, since patients who have or have had a marked dermatitis from any cause seem to me to be definitely predisposed to exfoliative dermatitis from arsphenamin, and the first injection may result in this most alarming of complications.

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[29] For an early experimental verification of this clinical impression see: Auer, J.: The Effect of Salvarsan on the Heart in Dogs, J. Exper. Med. **14**:248, 1911.

[30] Stokes, J. H.: The Protection of the Kidney in Intensive Antisyphilitic Treatment, with Special Reference to the Influence of Dental Focal Infections, Med. Clin. North Am. **3**:82, 844, 1919. Michelson considers this in the discussion on Guy, W. H.: Reactions Following the Administration of Arsphenamin, Report of Reaction in a Series of Twenty-Five Thousand Injections, J. A. M. A. **63**:901 (Sept. 20) 1919, in which exfoliative dermatitis is reported in association with a septicemia.

If due regard is paid to the necessity for a careful study of the patient before arsphenamin administration is begun, and the axioms governing its employment as I have outlined them are duly heeded, the incidental or secondary reactions to arsphenamin can be largely avoided. Primary reaction, as in the acute nitritoid crisis, arsphenamin gastro-intestinal disturbances, and the alarming and often fatal collapses recorded in the literature can be largely avoided[33] by a rigorously correct technic of administration, provided a reliable product is used. The tendency to blame either the drug or the patient for an accident should be restrained.[34] I have always felt it worth while to give the most painstaking attention to the preparation of water and of chemical reagents such as sodium hydroxid solution, to the glass, and lately, as a result of the investigations of Busman and myself,[35] to the rubber tubing. The tubing reaction has special interest in showing on what subtle details the outcome of an intravenous injection of any type may depend. I am emphatically in accord with Schamberg, McCoy and others [36] in insisting on adequate dilution and slow administration of arsphenamin solutions as essential to safety. We find the hyperalkalinization [37] by a quantitative as distinguished from a visual end-point technic to produce the disodium salt in preparing arsphenamin, very serviceable.[38] The use of solutions of arsphenamin which have strong odors, unusual colors when dissolved, or turbidity when they should be clear, is dangerous, nor does the manufacturer's claim that they have passed animal toxicity tests make them fit for use in man. While it is possible to be temperamental about mild gastro-intestinal reactions and unduly to modify dosage when they appear, it is worth recalling that most reactions can be done away with by the combination of correct administration with a fasting stomach and a cathartic twenty-four hours after injection.

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[31] Lier, W.: Ueber Abortivkur, Spirochätenreste und kombinierte Behandlung der Syphilis, München. med. Wchnschr. **61**:2233, 2276, 1914. For an interesting exception to this rule, in pneumonia complicated by syphilis, see Head, G. D., and Seabloom, J. L.: Arsphenamin in Pneumonia with Delayed Resolution in Syphilitic Soldiers, J. A. M. A. **73**:1344 (Nov. 1) 1919. For the Production of pneumonia in connection with the administration of acid arsphenamin see: Schwendtfeger, O. M., and Tinker, M.: Pneumonia Following Injections of Arsenobenzol, Am. J. Syphilis **3**:398, 1919.

[32] Potter, N. B.: Salvarsan in the Treatment of Double Infections, Tuberculosis and Syphilis, Am. J. M. Sc. **152**:823, 1916. Elliott, J. A.: The Treatment of Syphilis in Tuberculous Patients, Am. J. Syphilis **3**:291, 1919. Elliott notes especially the importance of the focal flare-up (Herxheimer). Burnham, E. A.: Syphilis of the Lung, Boston M. & S. J. **171**:411, 1914.

[33] For various methods of dealing with the nitritoid crisis, see: Stokes, J. H.: Atropin and Induced Anaphylaxis as a Protection Against Acute Arsphenamin Reactions, J. A. M. A. **72**:241 (Jan. 25) 1919.

[34] W. A. Pusey voices an expression of the opposite opinion in the discussion on Guy's paper (Footnote 20).

The highly embarrassing and fatal arsenical exfoliative accidents of arsphenamin, while not absolutely preventable, can be much reduced in frequency by preliminary removal of focal infections that tend to sensitize the skin, and by watching the patient for the first sign of irritation. This usually appears in the form of more or less general pruritus, with slight patchy dermatitis in the groin, neck and axillae and about the wrists and forearms. Such scrutiny should be redoubled after the fourth injection. Inunctions should not be used during the arsphenamin courses of patients who show a marked irritability, or give a history of dermatitis. The oatmeal and soda bath and administration of alkalis such as potus imperialis and Fischer's solution per rectum have seemed to me to be of value. Outright nephritis and anuria from a dose of arsphenamin has never occurred in my experience and is, I think, attributable to technical error.[39] Showers of casts are not infrequent, however, especially during epidemics of colds.

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[35] Stokes, J. H., and Busman, G. J.: Tubing as a Cause of Reaction to Intravenous Injection, Especially to Arsphenamin, Preliminary Report, J. A. M. A. **74**:1013 (April 10) 1920.

[36] Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-Arsphenamin, Second Communication, Arch. Dermat. & Syph. **38**:235, 1920. McCoy, G. W.: The Administration of Arsphenamin, J. A. M. A. **72**:1386 (May 10) 1919. Pusey, W. A.: Administration of Arsphenamin, J. A. M. A. **72**:1786 (June 14) 1919. Young, H. McC.: The Administration of Arsphenamin, Correspondence, J. A. M. A. **73**:131 (July 12) 1919. Goldenberg, H.: The Administration of Arsphenamin, J. A. M. A. **72**:1634 (May 31) 1919. Nelken, A.: Administration of Arsphenamin, J. A. M. A. **72**:1695 (June 7) 1919. Rieger, J. B.: The Administration of Arsphenamin, J. A. M. A. **73**:710 (Aug. 30) 1919.

[37] Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: (Footnote 10). Danysz (Footnote 6) Schamberg, J. F.: Caution Against the Use of Non-neutralized (Acid) Solutions of Salvarsan, J. A. M. A. **68**:1255 (April 28) 1917.

[38] McCoy, Footnote 36.

I have always been insistent on the principle of hospitalizing all arsphenamin cases until the time for most complications to develop is over, that is, for twenty-four hours. This does not protect against hemorrhagic encephalitis, which may not begin to appear for several days. On the arsphenamin service at the Mayo Clinic there have been two deaths attributable to the drug in 25,000 injections under such hospital control, among a difficult class of cases rather than among robust young adults, as in the army. One death might have been prevented had the patient been disposed to cooperate with us in the management of her focal infections. Once the operating room technic is perfected and the staff thoroughly impressed with every detail of indications and contraindications, the twenty-four hour rule may be relaxed to eight hours, if the patient is still under easy outpatient observation and can be hospitalized on the slightest sign of trouble.

USE OF ARSPHENAMIN IN NEUROSYPHILIS

Neurosyphilotherapy has furnished arsphenamin with a field for a number of its problems and for not a few of its triumphs. The frequency of neurorecurrence in the days before the appreciation of the dangers of insufficient arsphenamin, and the more or less theoretical neurotropism expected of the drug[40] by the mistake of regarding it as a species of glorified arsenic, has led to an unwarranted distrust of its efficacy. Neurotropism in the form of polyneuritis[41] is a reportable rarity, and the greatest overdosage has not, in my experience, been followed by such complications. I have perhaps felt that simple primary optic atrophy did not do well under arsphenamin. But as for the neurorecurrences, I feel that they would all but disappear from the field, if routine examination of the spinal fluid with the last arsphenamin injection[42] of each course were practiced. This would furnish us with sufficient warning and enable us properly to direct our treatment.[43] The rare exceptions would be those definitely neurotropic infections which respond unsatisfactorily to any treatment. It must be conceded, however, that in spite of its high value in neurosyphilis, occasional patients do not respond to the drug, and are even unfavorably affected. I have for example seen paresis in a period of remission forced into a rapid and fatal decline through ill advised arsphenamin enthusiasm. Massive mercurialization and large doses of iodids ranging from 500 to 1,000 grains daily will sometimes produce a response that no amount of arsphenamin can secure (arsenic fast organism?).[44]

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[39] Eberly, K. C.: An Unusual Case of Salvarsan Poisoning, J. A. M. A. **65**:1729 (Nov. 13) 1915. Woodyatt, R. T.: Hypertonic Salt and Alkali Solution in Salvarsan Anuria, J. A. M. A. **64**:1811 (May 29) 1915. Treatment of arsphenamin anuria with Fischer's solution.

[40] For experimental evidence suggesting the minor importance of the effect of alkaline arsphenamin on nerve tissue, see Joseph, D. R.: A Few Observations on the Action of Salvarsan on the Irritability of Nerve and Muscle, J. Exper. Med. **13**:634, 1911.

[41] Wolff, A., and Mulzer, P.: Zur Kasuistik der Behandlung der Syphilis mit Neosalvarsan (Arsenical Paraplegia), München. med. Wchnschr. **59**:1706, 1912.

I think it is no exaggeration to credit arsphenamin with having by one or another of its modes of administration reduced the mortality of parenchymatous syphilis of the brain to the point where it is no longer wise to attach an absolutely fatal prognosis to the clinical picture of paresis. In other words, only a therapeutic test with a fatal outcome now suffices to substantiate paresis as a clinical diagnosis. The redoubled arsphenamin therapeutic intensity, advocated by the late Dr. Southard and his associate Solomon,[45] has certainly in my experience transformed the clinical and serologic condition of many patients whom I would in earlier days have been disposed to abandon to their fate. Even granted that the ultimate outcome may be fatal, remissions of the most substantial kind can now be produced by intensive treatment in as high as 60 per cent. of patients who show only early signs of deterioration.

It is no longer asserted that intraspinal arsphenamin therapy, so long the center of schismatic and controversial discussion,[46] will accomplish the impossible. Rationally, it appeals to me as a local treatment of the central nervous system by combined antibody and spirillicide agents,[47] plus a mild antibody stimulating systemic therapy. The latter element is too often overlooked in estimating the benefit produced by the intraspinal part of this procedure. The success of the localizing measure does not justify a refusal to recognize the equally enduring and substantial benefits produced by systemic treatment. My belief that syphilis must be treated as a whole, rather than in parts, leads me to deprecate a panic-stricken rush for intraspinal measures the moment a syphilitic shows signs of involvement of the nervous system. In spite of the general safety of such methods as the Swift-Ellis-Ogilvie method of treatment, intraspinal treatment involves enough risks to make it a second rather than a first choice. Much more can be done to clear up neurosyphilis by general therapy than is generally realized.[48] Adequate attention to focal infection, urinary retention, and general hygiene alone, as suggested by Duke [49] and confirmed by my own experience, will often produce a response in what threatens to be a refractory neurosyphilis. I feel that where outright contraindications are absent, every neurosyphilitic, particularly in the early years of his infection, should have at least one stiff course of arsphenamin intravenously and inunctions or soluble mercurial injections before intraspinous therapy is even considered. I have seldom attempted both procedures together.

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[42] Stokes, J. H.: Three Cases Illustrating the Diagnosis and Treatment of Syphilitic Involvement of the Nervous System, Med. Clin. North Am. **3**:829, 1919.

[43] Swift advises a similar procedure in neurosyphilis under treatment: Swift, H. F.: Observations on Types of Response in Treatment of Syphilis of the Central Nervous System, Am. J. Syphilis **1**:524, 1917.

[44] Stokes, J. H.: Med. Clin. North Am. **3**:836, 1920.

[45] Southard, E. E., and Solomon, H. C.: Neurosyphlis, Modern Systematic Diagnosis and Treatment, Presented in One Hundred and Thirty-Seven Case Histories, Boston, Leonard, 1917.

[46] From the voluminous literature on the subject, it is well to read: Fordyce, J. A.: Truth About Intraspinal Injections in Treatment of Syphilis of Nervous System, A Reply, J. A. M. A. **69**:1482 (Nov. 3) 1917. Sachs, B.: Truth About Intraspinal Injections in Treatment of Syphilis of Nervous System, J. A. M. A. **69**:681 (Sept. 1) 1917.

The objection which applies to overenthusiastic estimates of the permanence of arsphenamin effects in other fields of syphilis applies to generalizations on its influence on the prognosis of neurosyphilis. Neither intraspinal nor intravenous measures will stop the drift toward an ultimately fatal outcome which some cases exhibit occasionally from the earliest weeks of the infection. Nor is the permanence of

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47. I do not feel that the mechanism of intraspinal effects and the relative merits of different technics are by any means settled by the mere demonstration of arsenic in the spinal fluid in varying percentages. For important studies on this question see Ogilvie, H. S.: The Intraspinal Treatment of Syphilis of the Central Nervous System with Salvarsanized Serum of Standard Strength, Report of Cases, J. A. M. A. **63**:1936, 1914. Swift, H. F.: A Study of Serum Salvarsanized in Vitro, J. Exper. Med. **24**:373, 1916. Barbat, J. H.: Permeability of the Meninges to Arsenic in Paresis and Tabes, J. A. M. A. **70**:147, 1918. Mehrtens, H. G., and MacArthur, C. G.: Therapy of Neurosyphilis Judged by Arsenic Penetration of Meninges, Methods of Treating Neurosyphilis, Arch. Neurol. & Psychiat. **2**:369, 1919.

48. Sachs, B.: On the Intravenous, Not the Intraspinal, Use of Arsphenamin in Syphilis of the Nervous System, Arch. Neurol. & Psychiat. **1**:277, 1919. Kaliski, D. J., and Strauss, I.: On Syphilis of the Nervous System, Pathological, Serobiological and Clinical Criteria with Especial Reference to Treatment, Am. J. Syph. **2**:609, 1918. Southard and Solomon, Footnote 45. Stokes, J. H.: Med. Clin. North Am. **3**:829, 1919.

49. Duke, W. W.: Multiple Infections, A Study of the Relation of One Infection to Another, J. A. M. A. **71**:1703 (Nov. 23) 1918.

the most brilliant results yet fully assured. To my mind, however, intraspinal therapy has a unique place as an addition to general measures in resistant early neurosyphilis and as a means of local approach to a neurosyphilis which is hedged about by contraindications in the later years of the disease.[50] The symptomatic advance of serologically negative cases in spite of intensive intravenous and intraspinal therapy is a well established fact and reflects equally on the efficiency of both methods. I must, however, confess a preference in cases of this type for the immunizing effect of small doses of neo-arsphenamin intravenously rather than for the more massive procedures. Of spinal drainage, I can only say that I have abandoned it as being no more effective than intravenous arsphenamin therapy alone.

USE OF ARSPHENAMIN IN PREGNANCY AND CHILDHOOD

In syphilitic pregnancy and childhood, arsphenamin should be widely used.[51] In the pregnant woman I agree with Wechselmann [52] that conservatism in dosage is imperative, even in acute early syphilis. I seldom find it advisable to exceed from one-half to two-thirds adult dosage. The combination with mercurial inunctions seems to me to be as well tolerated as mercury alone. In childhood, arsphenamin should be pushed with the same intensity in proportion to age and weight, and under the same contraindications that apply in adult life. Rectal arsphenamin medication seems to be as complete a superfluity as mouth administration [53] to one who can master the technical difficulties in treating children. In general, syphilis acquired *in utero* should be treated by the same combination of spirillicidal and immunizing technic which I have described for late syphils in adults. The symptomatic response of interstitial keratitis to arsphenamin is vastly better than to mercury in my experience, although I realize that ophthalmologists who are not in touch with syphilographers seem to make relatively little use of the drug. There are few phases of syphilis in which the tonic effects of arsphenamin and its value as a relief from continuous mercurialization are more striking than in the syphilis of childhood.

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[50] For an excellent and conservative statement of the possibilities of the method see Fordyce, Footnote 46.

[51] Holt, L. E., and Brown, A.: Results with Salvarsan in Hereditary Syphilis, Am. J. Dis. Child. **6**:174, 1913. Strathy, G. S., and Campbell, G. A.: Results of Treatment with Salvarsan in Late Congenital Syphilis, Am. J. Dis. Child. **6**:187, 1913. Simpson, J. W., and Thatcher, L.: The Treatment of Congenital Syphilis by Salvarsan, Brit. M. J. **2**:534, 1913.

[52] Wechselmann, W.: Kritische Bemerkungen zur Pathogenese eines "Salvarsantodesfalles," München. med. Wchnschr. **2**:1845, 1914.

[53] Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: The Administration of Arsenobenzol by Mouth, J. A. M. A. **67**:1919 (Dec. 23) 1916. These authors estimate mouth administration as therapeutically of little worth. On the other hand rectal administration is advocated by Araujo, S.: Arsenical Treatment of Children by Way of the Rectum, Brazil med. **32**:234, 1918; abstr., J. A. M. A. **71**:2113 (Dec. 21) 1918.

COMPARISON BETWEEN ARSPHENAMIN AND NEO-ARSPHENAMIN

Comparisons between arsphenamin and neo-arsphenamin still rest on uncertain and ill assorted data. I think it is safe to say that in general the dose for dose superiority of arsphenamin even on a basis of arsenic equivalency (4 dg. "606" equals 6 dg. "914") is conceded by syphilographers of large experience. It is my habit to estimate seven injections of neo-arsphenamin equivalent to five of arsphenamin. The charm of simplicity in the administration of neo-arsphenamin has drawn many adherents irrespective of the abstract merits of the question. Kolmer and Yagle's [54] recent emphasis on its nonhemolytic properties deserves further study, and may explain its lower reactivity in moderate doses. Yet my own experience compels the belief that neo-arsphenamin in the past has been more tricky and vasculotropic than arsphenamin, especially in large doses. Possibly the elimination of methyl alcohol from its manufacture will correct the difficulty.[55] In the meanwhile arsphenamin commands my personal confidence where radical effects can be secured.

USE OF ARSPHENAMIN IN NONSYPHILITIC DISEASES

The therapeutic applications of arsphenamin in other diseases than the spirilloses constitute interesting applications of its nonspecific or immunity stimulating action. My personal experience extends to its employment in tuberculids,[56] in glandular tuberculosis in the absence of syphilis, in blastomycosis,[57] actinomycosis and sporotrichosis, in streptococcus septicemia [58] and in intestinal infections with lamblia [59] and endameba. The effects of the drug have been discussed in the literature[60] in the treatment of anthrax,[61] malaria,[62] pellagra,[63] filarial infections[64] and trichinosis.[65] The rationale of the action of this drug in tuberculids as studied by Nicholas, Courmont, Gate and Carlet[66] is probably similar to its effect in other nonspirillar infections. These authors found that in patients with good resistance, a marked increase in the agglutinins for tubercle bacilli could be produced by the administration of arsphenamin. If the patient's resistance were low or falling, the effect was nil or bad. The methods of administration employed by these authors were not particularly effective and the action is in all probability more pronounced by a somewhat more energetic technic. The dosage in the treatment of all the above conditions should be moderate, and persistence is essential. The indirect action of the drug makes it impossible to predict in advance either the degree or the permanence of improvement. Very striking effects, however, are frequently produced. While the results are fairly constant in tuberculids, they are much more erratic in the mycoses and in the latter the method is in my experience no substitute for the intensive use of radiotherapy and iodids. My impression of the use of arsphenamin in septicemia is unfavorable. Lamblia infections treated by the technic

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[54] Kolmer, J. A., and Yagle, E. M.: Hemolytic Activity of Solutions of Arsphenamin and Neo-Arsphenamin, J. A. M. A. **74**:643 (March 6) 1920.

[55] Rieger, Footnote 36.

[56] Ravaut, P.: L'action du néosalvarsan et la réaction de Wassermann chez des malades atteints de tuberculides diverses, Ann. de dermat. et de syph. **44**:470, 1913. Tzanck, A., and Pelbois, E.: A propos du traitement des tuberculoses cutanées et des tuberculides par le néosalvarsan, Ann. de dermat. et de syph. **45**:65, 1914. Stokes, J. H.: Clinical Studies in Cutaneous Aspects of Tuberculosis. III. The Therapeutic Management of the Tuberculids, with Special Reference to the Efficiency of Arsphenamin, Am. J. M. Sc. **157**:522, 1919.

[57] First suggested to me by the late Frederick G. Harris.

[58] Brechot, A.: Neo-Arsphenamin in War Surgery, Paris méd. **9**:414, 1919; abstr., J. A. M. A. **73**:232 (July 19) 1919.

[59] Cade, A., and Hollande, A. C.: L'entérite à *"Giardia (Lamblia) intestinalis,"* Arch. d. mal. de l'appar. digestif. **10**:193, 1919. (This article includes the literature.)

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60. Wadhams, S. H., and Hill, E. C.: Three Cases of Amebic Dysentery Treated with Salvarsan, J. A. M. A. **61**:385, 1913. For a very good general summary, see Best, W. H.: The Use of Salvarsan in Nonsyphilitic Diseases, J. A. M. A. **63**:375 (Aug. 1) 1914.

61. Bettmann and Labenheimer: Ueber die Wirkung des Salvarsans auf den Milzbrand, Deutsch. med. Wchnschr. **38**:349, 1912. Gsell, J. L.: Neo-Arsphenamin in Treatment of Anthrax, Cor.-Bl. f. schweiz. Aerzte **48**:1505, 1918; abstr., J. A. M. A. **72**:77 (Jan. 4) 1919.

62. Stephens, J. W. W., Yorke, W., et al.: Studies in the Treatment of Malaria. XVI. Intravenous Injections of Novarsenobillon in Simple Tertian Malaria, Ann. Trop. Med. & Parasitol. **12**:211 1918-1919. Temporary Good Effect from Single Dose, with Relapse. XXV. Arsenic in Malignant Tertian Malaria, Ann. Trop. Med. & Parasitol. **13**:75, 1919. (Unfavorable Results from Novarsenobenzol.) Reed, E. U.: Two Cases of Malaria Treated with Salvarsan, U. S. Nav. Med. Bull. **9**:278, 1915.

63. Cole, H. P., and Winthrop, G. J.: The Status of Salvarsan in Pellagra, Based on the Reports of Twenty-One Collected Cases, J. A. M. A. **56**:1794 (June 17) 1911. (Forty-nine out of seventy-two cases recovered.)

64. Deschamps, M.: Neo-Arsphenamin in Filarial Chyluria, Bull. d. l'Acad. d. méd. **81**:655 1919; abstr., J. A. M. A. **73**:230 (July 19) 1919.

65. Best, Footnote 60 (Two unfavorable reports). Van Cott, J. M., and Lintz, W.: Trichinosis, J. A. M. A. **62**:680 (Feb. 28) 1914. (Unfavorable.) McNerthney, J. B., and McNerthney, W. B.: Trichinosis: Immediate Result Following Intravenous Injection of Neosalvarsan, J. A. M. A. **67**:1086 (Oct. 7) 1916. (Favorable reprot.)

66. Nicolas, J., Courmont, P., and Gate: Production expérimentale des agglutinines chez les animaux par les injections de salvarsan, Compt. rend. Soc. de biol. **73**:245, 1912. Courmont, P., and Durand, P.: Action des lavements de salvarsan sur certaines formes de tuberculose, Lyon méd. **121**:97, 1913.

described by Cade and Hollande (small intravenous injections) respond well, often in cases which resist all other methods, and the prospect of permanence seems to be fairly good. On the other hand, relapses are not uncommon and we are not yet convinced that larger doses and longer courses contribute anything to a satisfactory result. It is possible that the effect is produced by the elimination products of arsphenamin in the intestine rather than by the intravenous action of the drug itself, although the drug by mouth seems to be without effect.[67] I have known endameba infections, which seem to be more resistant and erratic than lamblia, to relapse after twenty-six intravenous injections.

The arsenical earmarks of late arsphenamin complications and ill effects should not lead one to think of the drug as arsenic in a therapeutic sense since it is a distinctly inferior and tricky substitute. The cacodylate delusion in syphilis probably had its origin in this uncritical analogy.[68] Occasional response in sarcoids and psoriasis has been noted. In secondary anemia of syphilitic origin the response is usually good. On the other hand, an unpleasant surprise in the form of a relapse with the assumption of primary characteristcs is not infrequent, and the case runs the course of a pernicious anemia. In cases of this type it is permissible to question the Wassermann reaction on which the diagnosis is usually based, since as Sanford [69] has suggested it is possible that false positive Wassermann reactions may occur in pernicious anemia. In bona fide pernicious anemias the action of arsphenamin used as a substitute for the customary administration of arsenic, is erratic and often unsatisfactory.[70] If the hemoglobin is below 30 per cent., in my experience it is wiser to transfuse before giving arsphenamin, since the effect of the drug used in first instance is less likely to be good where the hemoglobin is below the point mentioned.

The nonspecific actions of arsphenamin must be borne in mind in employing it for therapeutic tests to determine the presence of syphilis. Herxheimer-like reactions on first injection have been known to occur in lupus vulgaris in the absence of syphilis.[71] The rapid response of some tuberculids, especially erythema induratum, combined with the fact that by some technics these cases may show partial positive Was-

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67. Ravaut and Krolunitsky, quoted by Cade and Hollande (Footnote 59).

68. Cole, H. N.: A Study of Sodium Cacodylate in the Treatment of Syphilis, J. A. M. A. **67**:2012 (Dec. 30) 1916. This study effectually explodes this pernicious idea.

69. Sanford, A. H.: Diagnostic Methods in the Anemias, New York State J. M. **19**:415, 1919.

70. For a favorable report of twenty-four cases from which I doubt if a syphilitic factor has been fully excluded, see Bramwell, B.: The Treatment of Pernicious Anemia by Salvarsan and Neosalvarsan, Brit. M. J. **1**:406, 1915.

71. Herxheimer, K., and Altmann, K.: Ueber eine Reaktion tuberculöser Prozesse nach Salvarsaninjektion. Deutsch. med. Wchnschr. **37**:441, 1911.

sermann reactions, may lead to mistaken diagnoses of syphilis.[72] In malaria and anemias it is especially important to eliminate syphilis in estimating the effect of arsphenamin on the disease.

USE OF ARSPHENAMIN IN PROPHYLAXIS

No discussion of the applications of arsphenamin to therapeutics is complete without a mention of its possibilities in the prophylaxis of syphilis.[73] Where a known exposure has occurred within twenty-four hours I have employed two injections, given on successive days. The experimental aspects and possibilities deserve further study. It should be forcibly stated that such a procedure is under no circumstances to be employed later than forty-eight hours after exposure, nor is it ever to be employed in the presence of any suspected primary lesion. The use of arsphenamin for provocative procedures during the primary, Wassermann negative phase of a syphilis, or to treat genital lesions before a diagnosis is made, is attended with grave risks of confusion and complications, and should not be encouraged for general use as yet.[74]

CONSERVATISM IN USE OF ARSPHENAMIN

The last words of any discussion of the arsphenamins in therapeutics, should, I think, be an appeal for conservative interpretations. Particularly should such conservatism reign in the field of syphilis. Too short a time has elapsed since the discovery of these drugs, and too little is as yet known about the ultimate problems of the pathology, immunology and parasitology of syphilis, to justify the announcing of new infallibilities. The necropsy pathologist of the next fifty years may well, like Warthin, upset our most plausible generalizations of today. Seasoned tradition and conservatism are still the wisest guides in our interpretation of clinical cure. Arsphenamin has made it apparently possible and even probable, but only to the inexperienced has cure been made absolute and inevitable. I question, too, whether arsphenamin will prove to be the standardizer of the syphilotherapeutic field. We may prescribe minimum requirements for early cases, and if we do, let us place them, if anything, too far within the limits of conservatism. As for maximums, and for the adequate employment of arsphenamin in difficult cases, it will be a long day before a textbook guide and rule of thumb can pilot the inexperienced through a standardized routine to a guaranteed successful result. I feel strongly that it is a major duty of all to whom circumstances have assigned the material and the facilities for such work, to provide in time, by closer observation, by follow-up and by adequate record, for the exact data on which alone can be based a final evaluation of the arsphenamins in therapeutics.

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[72] This point is discussed with citation of the literature by Stokes, J. H.: Clinical Studies in Cutaneous Aspects of Tuberculosis. II. The diagnostic and Clinical Relations of Certain Tuberculids, Am. J. M. Sc. **147**:313, 1919.

[73] Magian, A. C.: Arsphenamin Prophylaxis of Syphilis, Bull. d. l'Acad. d. méd. **81**:675, 1919; abstr., J. A. M. A. **73**:230 (July 19) 1919.

[74] For the presentation in polemic form of the merits of this question, see Taege, K.: Salvarsanprophylaxe, München. med. Wchnschr. **66**:841, 1919. Riecke: Salvarsanprophylaxe, München. med. Wchnschr. **66**:969, 1919.

REPORT ON THE USE OF A PERMANENT SOLUTION OF ARSPHENAMIN

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Since the advent of arsphenamin, we have constantly had impressed on us the necessity of using the solution immediately after its preparation. The advantages of having a stock solution ready for use at all times must be known to every one, and do not require enumeration. From the point of view of public health, such a solution is of interest, as it will extend the benefits of arsphenamin to patients in communities where it has hitherto been unavailable. For the occasional user it will also remove the dangers which arise from imperfect technic in preparing the fresh solution.

The conception of a stock solution of arsphenamin which will remain nontoxic for weeks is so at variance with our previous experience that a brief description of the method of preparation of the solution used in this trial and known as solution of Arsphenamin-Lowy, will be of interest. The arsphenamin powder as received from the various manufacturers, is first tested biologically for toxicity and is required to be of a higher degree of purity than demanded by the United States Public Health Service. The water is freshly distilled, boiled and evacuated by means of a vacuum pump. The powder is then dissolved in either hot or cold water, depending on the brand used. This solution is placed under a vacuum to remove any gases which may have been present in the powder or generated during its solution. The acidity is then determined by titration and sufficient sodium hydrate added to form the disodium salt. The solution is then again placed under a vacuum for four hours, filtered into ampules and sealed under negative pressure, the object being to obtain a solution free from air and other gases.

The clinical trial of solution of Arsphenamin-Lowy, that I report, was made in the United States Public Health Service clinic conducted in conjunction with the clinic of the department of syphilis of the New York Skin and Cancer Hospital.

The ampules received by us contained 120 c.c. of solution of a dilution of 1 dg. to 20 c.c. of water, which is the dilution used in the clinic in preparing the fresh solution. The required number of ampules were opened and the contents filtered into a large flask and the gravity apparatus filled as required from this flask. The same method was used when handling the fresh solution. The cases were not selected, the solution being given to all patients in our customary doses of from 3 to 6 dg. to adults, and proportionately smaller doses to children. The number of consecutive doses varied from one to eight, at intervals varying from 3 to 6 days, depending on the patient's condition. A total of 850 intravenous injections were given and twenty-one intraspinal injections. The latter were given in doses of from 0.05 to 0.5 mg.

For the purposes of this trial reactions were considered to be any untoward or unusual effect occurring at the time of injection or complained of by the patient at his next visit. It is our routine custom to question each patient before treatment as to the effects of the previous treatment. In 5,819 injections of the fresh solution during the past fifteen months, there were 111 known reactions or 1.9 per cent.

In 850 injections of solution of Arsphenamin-Lowy, there were fifteen known reactions, or 1.7 per cent. Of the fifteen reactions, one patient complained of weakness after the first dose of 4 dg.; one received three doses without reaction and after the fourth dose of 4 dg. said he vomited all night and had pain in the back and headache; he received two doses of 4 dg. each, following this with no reactions; one vomited after the second dose of 4 dg., with no reaction after the next dose, which was also 4 dg.; five had headache only, with no reactions after the following doses: one had a slight diarrhea after the first dose of 3 dg., with no reactions later; one had nausea and a chill after the first dose of 3 dg., with no reactions later; one complained of dizziness after leaving the table, the dose being 5 dg.; one had a mild nitroid reaction after the second dose of 4 dg., with dizziness after the third dose of the same size and no reactions after subsequent doses of the same size; one had nausea and vomiting after the fourth dose of 5 dg., with no reactions later; one had a moderately severe nitroid reaction with vomiting after a dose of 3 dg. and gave a history of reactions after previous treatments elsewhere. There were no instances of skin eruption following the injections.

No unusual results followed the intraspinal use of the solution. A number of patients receiving intraspinal injections were treated in the dispensary and allowed to go home directly afterward.

While this test was instituted primarily to determine the toxicity of the solution for man, the various primary, secondary and tertiary lesions healed within the customary time.

One small initial lesion healed after the first dose; four others healed after from two to four doses. In one patient the macular eruption present entirely disappeared after one dose. In one instance of maculopapular eruption the macules disappeared after the first and the papules after the third dose.

Two cases of gummatous ulcerations of the face healed after four doses, and a large leg ulcer of over a year's duration improved after the first dose and was entirely healed after five doses. During the test no other treatment was given to any of the patients.

The Hygienic Laboratory has recommended a limit of thirty days' dating on the ampules after animal experimentation, but states that "in a general way, it may be said that if the solution is kept cool there is no appreciable increase of toxicity in the course of six weeks or two months."

CONCLUSIONS

1. It is possible to prepare a solution of arsphenamin which will keep long enough to be of practical use.

2. Observation thus far shows the solution tested to have a therapeutic value, apparently equal to that of the fresh solution.

10 East Sixty-First Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. RAIZISS, KOLMER, ROTH, STOKES AND STETSON

Dr. William Allen Pusey, Chicago: I was greatly interested in Dr. Raiziss' account of some of the faults of arsphenamin, and I admire the brave statement of the facts from him, a worker in the production of arsphenamin, that many of the troubles we get in the therapeutic use of the drug come from the drug itself. When a man dies from poison, like that of arsenic, after taking a dose of arsphenamin, it always does violence to my reason to have it emphasized that he must have died of some other cause, which has always been regarded as innocent and was never known to kill anybody before. It is highly interesting, therefore, to have Dr. Raiziss meet the issue squarely and tell us the damages he has found experimentally that arsphenamin produces.

While he showed from the experimental use of large doses in animals that arsphenamin itself has its potent dangers, Dr. Kolmer's paper supplements that of Dr. Raiziss in striking fashion by showing that many of the accidents from arsphenamin arise from changes in the drug due to manipulations or faults in technic in its administration, and thus we who administer it have responsibilities quite as heavy as are those of the manufacturer. He does not undertake to show that mishaps are invariably the fault of the physician, as some of the commercial exploiters of the drug would have it. He shows that the most common damage occurs in the kidneys and liver, and this confirms my impression. I was surprised to find that he did not find the damage in the meninges that we have learned to dread through the occurrence of hemorrhagic meningitis. I have come to the conclusion that the chief danger of arsphenamin in practical use is the danger to the kidneys. The only cases I can recall in which I fear I have done the patient actual harm have been those in which there has been the production of nephritis.

As to the comparative dangers of mercury and arsphenamin to the kidneys: On the basis of a purely clinical experience I cannot subscribe to the view that arsphenamin has less danger to the kidney than mercury. In my experience the therapeutic use of mercury pushed vigorously has shown little tendency to damage the kidney, whereas arsphenamin has shown considerable tendency to damage. I am familiar with the oft quoted statement that mercury has been found to be fifty times as poisonous to the kidney as arsphenamin, and I am ready to believe that 4 dg. of mercuric chlorid would be fifty times as dangerous to the kidney as 4 dg. of arsphenamin. It would certainly be dangerous enough. But we do not give mercuric chlorid in 4 dg. doses, and used in the doses that it is used, I am not able to subscribe to the claims of its great danger to the kidney.

I enjoyed Dr. Stokes' paper very much. In a general way I accept his creed. I am, however, not such a high churchman as he is, and my ritual is not so elaborate. I think he has given an excellent exposition of the therapeutic use of arsphenamin and one that accords with conservative judgment and experience.

Dr. William H. Guy, Pittsburgh: Since the introduction of the arsenicals a voluminous literature has grown up, but nothing more important has been presented at any one time than we have heard today. In the application of any therapeutic agent an attempt is made to obtain a therapeutic victory with as little damage to the patient as possible, and the way is paved to success along those lines when facts displace theory and conjecture regarding the use and limitations of any drug. In Dr. Raiziss' paper the question of the toxicity bearing on the impurities is interesting because of the fact that he has arrived at some conclusions, as yet indefinite, that there must be some small impurity, such as was reported by Drs. Schamberg, Raiziss and Kolmer before. I think most of us will agree that certain lots of the drug are more toxic than others, and that it is very difficult to account for the reactions except by the content in the drug of some unknown impurity.

The paper of Dr. Kolmer is interesting because of the fact that while it shows very definite pathology in the dosage given, it also demonstrates that in doses ordinarily used therapeutically, while not free from danger, arsphenamin is comparatively safe. The relative toxicity of acid, monosodium and disodium arsphenamin is clearly demonstrated. It behooves us to use a technic that will avoid the pitfalls pointed out.

Dr. Roth's paper raises the question of foreign and American products, and it is very gratifying to know that we can manufacture a product far superior to any foreign product.

What constitutes immunity in syphilis is a difficult question. I believe it is fair to say that the only real immunity in syphilis is that conferred by an uncured infection. If any real immunity is created following a cure in syphilis, it certainly is short lived.

Dr. Elliott's conclusions agree with clinical experience. His reference to the reactions reported in connection with my experience in the army leads me to say that I cannot definitely state whether or not new tubing was responsible. Certainly, the fact that Dr. Stokes' clinical picture agrees so closely with mine makes it suggestive. The one thing that was found at the time was the fact that a new still had been installed with lead and copper lining. The fact as shown by Emery that arsphenamin is increased in toxicity by these two metals we thought to be significant. The use of a standard preparation of arsphenamin has its advantages for the man who is far from the beaten paths because it relieves him of many ordinary difficulties. Against it is the fact that most of us do not have need of it and that most of the technical difficulties are overestimated; also there is greater expense in using the drug in that manner.

Dr. Richard L. Sutton, Kansas City, Mo.: In all cases of syphilis we must study the patient as well as his disease. We must build up his resistance to the highest possible point. I have repeatedly seen cases in which it was apparently impossible to secure a negative serum test promptly become negative following the removal of some concomitant focal infection, or following a good physical and mental rest. While the remedy is not a specific in pemphigus, I have had excellent results following its use in several instances, especially when injected intramuscularly, so that the patient will secure the benefit of prolonged arsenical medication. In dermatitis herpetiformis, lichen planus and psoriasis, arsphenamin has proved of little or no value in my hands. It is extremely simple to prepare a solution of arsphenamin. An intelligent nurse can learn how to do it in about twenty minutes. I feel that any physician who has not skill enough or initiative enough, or sense enough to mix his own preparations had better leave so powerful a drug alone.

Dr. Augustus Ravogli, Cincinnati: Many physicians begin with intravenous injections of arsphenamin in 0.2 or 0.4 dg. doses, giving one injection per week. I do just the reverse. I begin with 0.6 dg. and give three injections of 0.6 dg. each every two or three weeks and then I reduce the dose. I think the best way is to give a large dose in the beginning and then decrease. In a very few days the hard chancre melts away. I have never had any untoward effect. I never use gray oil more than once a week, from 6 to 8 minims at each injection.

Dr. Ernest L. McEwen, Chicago: I was glad to hear Dr. Roth speak about the danger of shaking the solution of neo-arsphenamin. Reasoning from the statements that are made relative to oxidization of this product, I have always felt there must be some danger in agitation to effect solution, but I never could get any authoritative information on the point. Having had a very bad reaction from a certain make of neo-arsphenamin, I wrote the manufacturers asking them how much danger there was in shaking to bring the powder into solution. They replied that with a short period of agitation there was no danger, but prolonged shaking might produce harmful changes. I also asked them how much danger there was in leaving the solution exposed while preparing the patient; they replied that under ordinary conditions half an hour was perfectly safe. In a case of oriental sore, two doses of arsphenamin were given without any effect whatever.

Dr. Charles M. Williams, New York: I agree that it is essential to make a positive laboratory diagnosis of any sore before starting treatment, but in some cases it is not as essential to do this as to get the man cleaned up. In some instances, as in army camps, large bodies of men are removed from laboratories and microscopes and other necessary equipment, and the important thing is to get them cleaned up. I believe, therefore, that there are exceptions when one is justified in beginning the treatment at once in cases in which the diagnosis is based on clinical findings only.

Dr. George W. McCoy, Washington, D. C.: Were the toxic results reported from arsphenamin of commerce or from rejected lots? In other words, had they passed through the hygienic laboratory test or did they represent something else. With respect to foreign products, I am sure it is not very generally understood that arsphenamin and neo-arsphenamin may not be imported or sold or manufactured in the United States, except in establishments having a government license. Recently, several establishments abroad asked for licenses, and we have a man in Europe now who is investigating these establishments, and if they are found to meet the standard, a license will be granted. The failure to do this before has had no great influence, for, as the papers presented here have shown, there is plenty of high grade arsphenamin in the United States. If the United States grants licenses, there is still a question whether producers in foreign countries would have a right to ship these arsenicals into this country because the patents for all these preparations have been sold to a corporation, the Chemical Foundation. The best legal information seems to indicate that the rights of the Chemical Foundation to those patents are valid.

In relation to the quality of the drug of American make: More than two years ago we began to get reports from the venereal disease clinics, covering thousands of cases every year, and it has come out definitely that the reactions from arsphenamin and neo-arsphenamin were almost invariably associated with improper technic of administration. You might be surprised to find how often arsphenamin is given without adequate dilution and how often the dose is injected into a vein in from thirty to sixty seconds. Another thing is that hot water is required for the preparation from one American laboratory, while to use hot water with other American preparations increases the toxicity very decidedly. All the instructions that go with these latter preparations warn against using hot water, and yet frequently we have had reports of bad results from that.

In respect to arsphenamin in solution, I hold no brief for it. When the matter was brought to our attention several months ago, I thought considerable risk was involved. We consulted pharmacologisst and chemists as to the advisability of issuing a license for anything of that sort. Then we got the producer to come to the Hygienic laboratory and demonstrate the method of manufacture, and after much consideration it was felt that so far as we could determine the preparation was, at least, relatively free from risk and a proper one for license.

Dr. Harold N. Cole, Cleveland: I disagree with Dr. Williams. I think it inadvisable for this Section to go on record as advising any general practitioner to treat any sore until a diagnosis of syphilis has been made. I agree with Dr. Sutton that the man who cannot mix his arsphenamin or neo-arsphenamin should not give it. He has no right to do so. Too many cases of syphilis are being treated by men who have no right to treat syphilis, and the results will show in the next generation.

Dr. Julius Grinker, Chicago: I have used concentrated solutions of neo-arsphenamin hundreds of times in cases of nervous syphilis. I have shaken the bottles and I have yet to see a bad reaction, except those we see occasionally. I see no difference in the effect between concentrated and diluted solutions. As regards arsphenamin in permanent solution, I have had an opportunity of trying about sixty or seventy ampules of this preparation at the Cook County Hospital, and neither I nor my interns have been able to report a single bad reaction. I am convinced, therefore, that those who have no means of preparing the arsphenamin or neo-arsphenamin can now treat syphilis. I cannot help but disagree with Dr. Sutton; because a man cannot take out a tumor of the brain does not mean that he cannot diagnose a tumor of the brain and direct its removal, and that because a man cannot give an injection which a trained nurse can give, he has no right to treat syphilis. If a solution is handed to him for the treatment of syphilis, and that solution has been proved to be without risk, there is no reason why he should not use it for the benefit of his patient.

Dr. Alec N. Thomson, Brooklyn: From the viewpoint of the propagandist who is endeavoring to get better treatment and earlier diagnosis for the syphilitic patient through the medium of the general practitioner, I think we should emphasize what Dr. Grinker, Dr. Cole and Dr. Williams said. This information should be placed before the entire medical profession in an effort to get better diagnosis and earlier treatment.

Dr. J. N. Roussel, New Orleans: I wish to call attention to the wonderfully beneficial effect of arsphenamin in the treatment of plantar warts. I have warts treated ineffectively, recur and disappear within ten days after one 0.4 dg. dose of neo-arsphenamin.

Dr. Marion H. Foster, Alexandria, La.: One should never agitate arsphenamin vigorously while mixing. Reactions will follow if it is done. After giving about 1,800 injections, I have concluded that neo-arsphenamin is not nearly as reliable in the treatment of syphilis as arsphenamin, and I do not use the former if the latter is obtainable. Nothing has been mentioned concerning the complete rational treatment of syphilis, which, of course, includes more than medication by arsenic alone. Although it is the great spirocheticide, arsphenamin cannot become operative against organisms buried in massed indurations until these areas are sufficiently obliterated by the use of iodin to tolerance, and this influence is just as essential for the induration of the primary chancre as it is in indurations of the later stages, for the reason that the pathology of obliterative endarteritis is common to all.

Dr. Otto Lowy, Newark, N. J.: As the man responsible for solution arsphenamin-Lowy, I take exception to some of the statements made, namely: That the physician who cannot prepare an arsphenamin solution has no business to treat syphilis. This statement would be all right if medical colleges and state boards of licensure would insist that medical graduates cannot practice medicine until they are fully qualified to prepare these solutions properly. Furthermore, as long as older physicians, who have neither the facilities nor the experience to prepare arsphenamin solutions, are permitted to practice medicine, the dictum laid down by Dr. Sutton and others cannot hold. It is all right for the gentlemen who have all the proper facilities, such as nurses, stills, time, etc., at their disposal to say that they do not need a ready made solution, but how about the country practitioner? Is his patient to be permitted to infect the entire community because he cannot mix arsphenamin and therefore should not be permitted to treat the infected individual? Or would it be better to have the doctor go to the roundhouse to take the water from the exhaust of the locomotive or to the icehouse to receive his distilled water? Solution arsphenamin-Lowy has not been prepared to popularize the treatment of syphilis, but to put into the hands of qualified practitioners of medicine a safe solution of arsphenamin.

Dr. M. J. Farber, St. Joseph, Mo.: Shall a country practitioner who has no familiarity with the technic of administration of these drugs be barred from administering them? Is it the toxicity of the drug that makes it impossible? Or is it the administration of the drug by an improper method? If a patient is killed by improper methods, by unhygienic technic, or undistilled water, shall we put the fault on the manufacturer of the drug, or lay it to the unskilled administration of the drug? Shall we today indiscriminately administer the drug before finding out if the disease is syphilis? Or whether a primary sore is a chancre or not? We should install in every city, town and village a society for the prevention of social diseases to which a patient can be sent for a diagnosis. Dr. Sutton is right in saying that the man who cannot prepare his own solution of arsphenamin or neo-arsphenamin should not meddle with it. If he does not know the dose of a toxic drug, surely he is not going to administer that drug before inquiring what the dose is and how it should be administered.

Dr. Arthur W. Stillians, Chicago: I suggest that Dr. Reasoner add tuberculid to the list of nonspecific diseases that can be treated very successfully with arsphenamin. I have seen some very excellent results in cases that had resisted other methods. I wish Dr. Stokes would tell us what his objection is to the alternation of arsphenamin and mercurial treatment.

Dr. W. D. Calvin, Fort Wayne, Ind.: A man who cannot make a venepuncture or who cannot learn how to administer arsphenamin had better have his diploma revoked. I object to some of the views expressed by some of the speakers because of the reflection on the general profession. I can conceive of men so situated that it is not easy to prepare these solutions. If the manufacturers have arrived at that accuracy so that a preparation of arsphenamin can be prepared in a form that is not objectionable, I think I will use this preparation in the future, although, as a rule, I mix my own preparation. If it is true that so many of the population are syphilitic, as has been stated today, and we must rely on those who are expert in administering this treatment, we will have a large percentage of the syphilitics going untreated. That would be decidedly unfair. Therefore we should be more lenient in our criticisms of the preparation of solutions by the manufacturer.

Dr. Walter J. Highman, New York: I was much interested in Dr. Reasoner's paper, particularly in connection with ratbite fever, a disease which should be known by the dermatologist, for some of its features suggest erythema perstans. I am not surprised that Dr. Reasoner has not mentioned pemphigus. I have seen many cases and arsphenamin, as all other therapy, has been useless. In regard to plantar warts, I wonder whether Dr. Roussel made a Wassermann test in those cases in which the warts so rapidly disappeared after arsphenamin was given. However, the most important questions are those of arsphenamin reactions, and the use of permanent solutions. In at least two instances, I think that death might have been unjustly ascribed to arsphenamin.

In regard to the permanent solution of arsphenamin, Dr. Calvin has so completely expressed my views that there is little for me to add. I do not take the attitude of Dr. Sutton, but think that whenever anything of this sort comes into existence we should, at least, try it before condemning it, because the only hope of eliminating syphilis is to make its management easy. If 8 per cent. of our population are syphilitic, as has been brought out, and I think it is nearer 18 per cent., we have not trained syphilographers enough to meet the demand. Unless some one comes to the rescue and simplifies therapy, we will not be able to treat syphilis in bulk, and the social problem of treating syphilis is to inundate syphilitics with arsphenamin, as well as mercury. A permanent solution of arsphenamin will aid in this campaign.

Dr. Paul E. Bechet, New York: It might be possible that toxicity is increased either by the concentrated (from 5 to 10 c.c.) hand syringe method, or the use of dilutions of 120 c.c. and over. The natural tendency with the hand syringe is to give the injection too rapidly. It seems plausible that rapidity of injection plus concentration would tend to increase accidents. On the other hand, excessive dilutions increase the so called "water faults." In my experience, reactions are greater with overdilution or concentration than with dilutions of from 60 to 80 c.c. to a full dose, given by the gravity method. Since adopting this dilution, with the usual other precautions rigidly observed, I have not had a single reaction, slight or otherwise, for the preceding two years.

Dr. George P. Lingenfelter, Denver: Is the arsphenamin solution mentioned really permanent? My understanding is that it is supposed to last only about four weeks.

Dr. Cary Eggleston, New York: While I am generally opposed to embracing new products and recognize the fact that there is often an excess of enthusiasm on the part of their manufacturers, nevertheless, looking at it from the point of view of the man who does not devote his entire time to dermatology and syphilography, I feel that, perhaps, there is need for a well prepared, easily administered solution of arsphenamin. In the rural districts and small towns where skilled syphilographers are not present, it seems to me that we should encourage the physicians who are there to handle syphilis to the best of their ability, and that we should make their usefulness as great as possible by relieving them from more or less difficult technical matters. We should encourage their use of arsphenamin and thereby increase the effectiveness of the treatment of syphilis. It has seemed to me that the criticisms have been made from the personal point of view; that is, the viewpoint of the man with the well equipped laboratory who is administering a large amount of arsphenamin every day, and not from the point of view of the man who occasionally treats syphilis under unfavorable circumstances. If a commercially prepared stable solution of arsphenamin is shown to be without danger, I, for one, believe we should urge its use and lend it our support.

Dr. W. T. Watson, Baltimore: I do not live "on the frontier," but yet this prepared solution appeals to me very much from the point of view of saving my time. I can get freshly distilled water, and I have no trouble whatever with my technic, but it is time consuming and I am always hunting for ways of saving time.

Dr. George W. Raiziss, Philadelphia: I was glad that Dr. Pusey appreciated the position we had taken in reference to the search for truth as far as arsphenamin is concerned. Much has been written on the pathology and clinical experience with arsphenamin and neo-arsphenamin, but little is known of the chemical composition of these drugs. How close to the theoretical formula is the drug as used in practice today? Dr. Guy mentioned the indefiniteness of the results. The results are definite, but the work is not yet complete. I found that in order to appreciate the composition of arsphenamin, we must not be satisfied only with the official requirements of arsenic analysis. Other elements must be sought for. I found definitely that as far as the relationship of the arseno group to the amino group is concerned, we are dealing with an exceptionally pure compound. The same cannot be said of neo-arsphenamin. It is surprising to find that so little is known of the chemistry of neo-arsphenamin. Experience has shown that shaking the water solution of arsphenamin before the addition of alkali produces but very little oxidization. I have always emphasized the undesirability of unnecessary exposure of the alkalinized solution of the drug to air.

Dr. John A. Kolmer, Philadelphia: While necropsy reports indicate the production of serous and hemorrhagic meningitis in Europe, in this country meningeal changes have been much less conspicuous and generally absent. Our experimental animals frequently showed congestion of the meninges and some intracerebral hemorrhages, particularly after the injection of acid solutions and to a lesser extent after alkaline solutions, but the American made arsphenamin does not appear to produce the meningeal and cerebral changes reported in fatal cases in Europe. All of our studies were made with arsphenamin and neo-arsphenamin that had passed the official toxicity tests, namely, 100 mg. per kilo of arsphenamin and 200 mg. per kilo of neo-arsphenamin. I wish to emphasize the practical and important relation of concentration of solution of arsphenamin on the results of toxicity tests. In our early tests we were accustomed to inject rats and rabbits with a piston syringe, and following a natural tendency when using a syringe the injections were made rather rapidly. Under these circumstances arsphenamin was considered satisfactory if an animal survived 50 or 80 mg. per kilo. When we began injecting rats with a gravity apparatus, we found that tolerance was appreciably higher. I am absolutely convinced that the rapid injection of concentrated solutions of arsphenamin increases the percentage of reactions and that the diluted form is preferable for administration to persons. Dr. Schamberg, Dr. Raiziss and I have compared the two compounds by extensive series of trypanocidal tests, employing rats. The microparasite used was a strain of *T. equiperdum* that is fatal for white rats in about six days. To prevent trypanosomiasis and save the life of the animal it is necessary to administer about 20 mg. per kilo of body weight of arsphenamin; to accomplish the same with neoarsphenamin it is necessary to inject about 40 mg. per kilo of body weight. Insofar as these trypanocidal tests are concerned, arsphenamin has about one and three-quarter times the therapeutic effect of neoarsphenamin and we cannot really say that 0.9 gm. of neo-arsphenamin is equivalent in therapeutic activity to 0.6 gm. of arsphenamin. Relative to the toxicity of the two drugs, they have varied considerably in our laboratory. About six months ago Dr. Schamberg, Dr. Raiziss and I conducted a large series of comparative tests with arsphenamin from six laboratories, finding that they varied in toxicity for rats in doses ranging from 80 to 140 mg. per kilo. The general average was 105 mg. per kilo. With neo-arsphenamin the results were from 180 to 300 mg. or more per kilo of body weight. The general average was about 254 mg. per kilo. Neo-arsphenamin therefore, is much less toxic than arsphenamin, and I believe should be given in larger doses than customary, or, at least should be given at shorter intervals in order to obtain the same therapeutic effects secured from arsphenamin. In regard to the dilution of neo-arsphenamin, my remarks referred only to arsphenamin. So far as I know, 0.9 gm. of neo-arsphenamin may be administered dissolved in from 5 to 10 c.c. of water with safety and satisfactory results.

Dr. George B. Roth, Washington, D. C.: Too little attention is paid to the relative instability of neo-arsphenamin and arsphenamin. I have commonly observed that the various preparations vary greatly in their toxicity. One may have a minimal lethal dose of 180 mg. and another of 80 mg. per kilo. Now if we take a high grade arsphenamin and mistreat it by shaking, for instance, we are bound to get bad results on administration. However, high grade arsphenamin should stand more mistreatment than a relatively low grade product. Original toxicity as well as decomposition must both be considered when we talk about the impurities of arsphenamin. I want to emphasize the fact that neo-arsphenamin, especially, is a very unstable substance and when shaken as an aqueous solution, in the presence of air, it becomes highly toxic, presumably from the formation of "arsenoxid." Some lots of neo-arsphenamin seem to be especially "sensitive" and become toxic more readily than others. Some speakers have credited me with saying that neo-arsphenamin should be discarded. The statement I made was, that relatively difficultly soluble neo-arsphenamin should be discarded. This conclusion was reached because, in our experience, such preparations killed about 90 per cent. of the animals, and so we look on difficultly soluble neo-arsphenamins as very dangerous products.

Dr. John H. Stokes, Rochester, Minn.: I have always felt that the kidney was the most abused and least appreciated factor in the treatment of syphilis. I think we have made 30,000 examinations of the urine, many blood urea examinations and renal function tests, and I have yet to see satisfactory evidence that arsphenamin is more toxic to the kidney than mercury. Indeed, I have seen every evidence that the reverse is the case. Schamberg, Raiziss and Kolmer have also estimated that the toxicity of mercury is about fifty times that of arsphenamin. Dr. Elliott's work follows the logical approach to the question of arsphenamin effects. In both the one injection and two injection a week method of giving arsphenamin there was very little evidence that the kidney was at all affected. It is a misfortune to have to use such a word as "immunize." We know very little about the nature of resistance to syphilis, although agglutinins for the *Spirochaeta pallida* are known. In regard to Dr. Foster's comment on neo-arsphenamin, there are not sufficient data on which to base a true idea of its clinical value. I depend on arsphenamin for radical results. I disagree emphatically with Dr. Williams. The practices of military life should not be transferred root, stalk and branch to the conditions of civil life. It would be a misfortune if word should go forth from this section that early lesions should be treated on sight and without careful diagnosis. You will find a polemic in the *Münchener Medizinische Wochenschrift* in which every side of the question is discussed. As to Dr. Stillians' question, I see no objection whatever to the alternate use of mercury and arsphenamin in suitable dosage. I simply stated that I thought it advisable in the earlier stage of the infection to use them synchronously, but that later in the disease I used them alternately.

Regarding Dr. Lowy's preparation, I want to congratulate him for the way he has brought it to the attention of the profession. After testing 500 doses of the solution I must say that I do not like it as well as the preparation we make ourselves on the spot. It seems to be more alkaline and to produce thrombosis quite a good deal oftener, and this is important in a one vein arm. I feel, too, that it produces more gastro-intestinal reactions than freshly prepared arsphenamin. I feel that it will deservedly have great vogue and I hope that Dr. Lowy will carry through his entire sales organization, to the very last man, the high principle which he has put into its introduction to the medical profession. I know that it has been proposed as a selling argument for such a preparation that it will make it unnecessary for the general practitioner to use the judgment of experts. I do not think it should be sold as a means of keeping syphilitics out of the hands of experts, but that it should be a means of enabling the expert to extend his influence to the farthest point of the field, by securing better technical cooperation from the average physician. Dr. Nichols, have you had any experience with the use of arsphenamin in sprue?

Dr. Dudley D. Stetson, New York: It is not within my province to argue either for or against this solution. It is well known that many physicians are using various substitutes for arsphenamin simply because these substitutes come to them in ampules ready for injection. If instead of doing this they can be brought to use arsphenamin, a world of good will be accomplished. As to the keeping qualities, the Hygienic Laboratory has placed a limit of thirty days on the solution, and this limit should be observed. I have used a few ampules kept for six weeks at room temperature with no bad results, but this is not recommended. Dr. Lowy informs me that he has kept the solution in a refrigerator for six weeks and found that it would still pass the required test for toxicity.

Dr. Henry J. Nichols, Washington, D. C.: In the treatment of plantar warts we have had no experience and are not familiar with any other references. If arsphenamin is so efficient, and if warts are infectious, it is possible that they may be due to spirochetes, or the Wassermann reaction may have been positive in these cases. We have a number of cases of sprue, and arsphenamin has been used, but not systematically. The results of sporadic use have not been encouraging.

We overlooked pemphigus. I recall a number of references in the older literature, but had not seen anything recently on it. The point we wished to emphasize was the group action of arsphenamin in spirochetal diseases. In spite of the "advanced state of our knowledge," we have a subconscious feeling that syphilis is a peculiar disease. However, from a conscious point of view, we know that treponema pallidum is not essentially different from any other pathogenic micro-organism, and the sooner we overcome our subconscious attitude and realize that syphilis is an infectious disease just like any other, the better we will be qualified to treat it. This point of view is reached by considering syphilis as one of a group of spirochetal diseases. Another subconscious idea we have is that arsphenamin has a peculiar effect on *Spirochaeta pallida*. This idea is also a mistaken one, because in the beginning Ehrlich worked with a group of four diseases due to spirochetes—relapsing fever, fowl spirochetosis, yaws and syphilis—and more nearly succeeded in curing the other three of these diseases with a single dose than he did syphilis. There is something to learn about arsphenamin, therefore, in considering its effect on diseases due to other spirochetes than *Spirochaeta pallida*. If I may be permitted to summarize the discussion, I would emphasize the following points: First, in regard to reactions, there have always been some complications in the use of arsphenamin. From today's symposium it is clear that the drug itself may be at fault, and that we must demand a high standard of purity. Also, it is evident that the tissues may be damaged even by a pure product under certain circumstances. The man who is giving the drug has much responsibility in regard to reactions, and the following rules must be observed: (1) arsphenamin must be made alkaline beyond the point of solution of the neutral salt so that the disodium salt is formed; (2) it must be diluted properly; and (3) it must be given slowly, and must not be shaken after it is in solution. Finally, a number of points about the therapeutic plan and the individual patient must be considered. When all of these possibilities are provided for, we can and do obtain wonderful and brilliant results.

In regard to the relative value of arsphenamin and neo-arsphenmanin: Neo-arsphenamin is easier to give, and possibly less toxic, but it has not the punch of arsphenamin, either in clinical or serologic results. However, manufacturers are making about seven times as much neo-arsphenamin as arsphenamin. This means that there is a demand for a drug which is easier to give. If it is true that arsphenamin is the best drug, there is some justification for the trial of the Lowy preparation. This preparation has been licensed by the Hygienic Laboratory, and it should be given a trial. In regard to the criticism that drugs should be prepared only by the man who is going to use them, I venture to say that there are a number of men who give vaccines and serums without knowing any more about them than the man who uses the Lowy preparation knows about that. Undoubtedly syphilis is best handled by persons who understand and can control the technic of arsphenamin preparation, but there may be a certain field for arsphenamin solution ready for use. I am particularly interested in arsphenamin because I gave the first dose given in the United States, in the Spring of 1910, at the Rockefeller Institute, and I have worked on the subject more or less ever since. The last ten years have seen a great improvement in the method of handling syphilis by American practitioners, and they have also contributed a great deal to the elucidation of the proper use of arsphenamin.

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POLYNEURITIS PLUS DERMATITIS EXFOLIATIVA FOLLOWING NEO-ARSPHENAMIN *

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The list of phenomena which have been observed following the administration of arsphenamin and neo-arsphenamin is a lengthy one. I shall not attempt to add anything new to this subject, but I wish to emphasize a syndrome the rarity of which is attested to by a review of the literature as well as in personal communications from a number of syphilographers.

To attempt to deal adequately with both polyneuritis and exfoliative dermatitis would be, I believe, too great a task for a paper of this character. For the sake of brevity, because of its infrequency and also in order to give it deserved prominence, I shall therefore confine myself almost wholly to a discussion of polyneuritis. I shall refer not only to cases following the use of arsphenamin and neo-arsphenamin, but I shall mention also other instances due to arsenic, as well as to syphilis and mercury.

CASES OF ARSENIC POLYNEURITIS REPORTED IN THE LITERATURE

The association of polyneuritis and dermatitis exfoliativa following the arsenical preparations just referred to was first mentioned by Duhot[1] in 1912. In patients treated according to Schreiber's technic using large doses of neo-arsphenamin, 1.2 to 1.5 gm. repeated every two or three days until four or five injections had been given, he observed the following syndrome: At first the patients complained of formication and pain in the soles and calves. The feet and legs became edematous, the skin reddened and a furfuraceous scaling appeared. When the trouble was of a more serious nature the successive disappearance of the plantar, Achilles and patellar reflexes was noted. There were cramps in the calves associated with a loss of muscular power in the legs and even paralysis. Similar but less

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[1] Duhot: Etude préliminaire et expérimentale sur le neosalvarsan ou préparation neutre de 606, Rev. belge Urol. et de Dermato-Syph. **1**:91, 1912.

marked symptoms appeared in the hands and arms. There was no evidence of rectal or vesical disturbance. Duhot saw five cases of this kind and believed them all to be due to chronic arsenical intoxication. None of his patients showed evidences of cerebral involvement or disorders of sight or hearing. The nervous symptoms appeared from two to three weeks after the completion of the treatment. Later Duhot emphasized the importance of an examination of the reflexes before inaugurating neo-arsphenamin treatment. In over 1,200 patients, to whom about 9,000 injections of arsphenamin were given, he saw no such nervous symptoms. Both Ehrlich and Wechselmann [2] at an early date emphasized arsenical neuritis following neo-arsphenamin treatment.

Spillmann [3] reported a case of scarlatiniform erythema plus polyneuritis following two injections of neo-arsphenamin given ten days apart. The first injection, 0.40 gm., was followed by fever, headache and diarrhea. Two hours after the second injection (0.3 gm.) the patient became violently ill, exhibiting high fever, pulse of 150 to 160, severe headache, diarrhea and other symptoms. The erythema appeared next day and soon spread over the entire body. Symptoms of polyneuritis appeared in the legs five weeks later and were soon followed by paralysis of the left facial nerve.

Latham [4] and Carr [5] have recently reported in our literature fatal cases of dermatitis exfoliativa after arsphenamin treatment. In a personal communication, Dr. Fordyce has mentioned a case analogous to ours, which he saw in consultation. It was an exfoliative dermatitis following arsphenamin treatment in which multiple neuritis appeared about six weeks after the dermatitis had cleared up. Drs. Ormsby and Howard Morrow also informed us that they had observed examples of this syndrome. Drs. Charles J. White, S. E. Sweitzer, Everett S. Lain and Udo J. Wile have observed polyneuritis following these drugs. Dr. Shelmire has seen a patient in consultation who presented exfoliation of the skin plus icterus and a generalized purpura following two arsphenamin injections. It appears that exfoliative dermatitis has been observed by a large majority of those whose experience with these preparations has been extensive.

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[2] Wechselmann: Ueber Neosalvarsan, München. med. Wchnschr. **59**: 2099, 1912.

[3] Spillmann, L.: Un cas d'intoxication arsenicale suraigue à la suite de deux injections de Neosalvarsan, Bull. Soc. franç. de dermat. et syph. 100, 1914.

[4] Latham, J. R.: Exfoliative Dermatitis Due to Arsphenamin. Report of a Fatal Case, J. A. M. A. **73**:14 (July 15) 1919.

[5] Carr: Exfoliative Dermatitis Following the Administration of Salvarsan, Proc. Med. Assn. Isthmian Canal Zone **10**:115, 1917.

Brooks and Roberts[6] have thoroughly described the cutaneous manifestations following the epidemic of arsenical beer poisoning in England during 1901. The symptoms observed corresponded closely to those seen after arsphenamin and neo-arsphenamin treatment. Exfoliation of the skin, pigmentation, hyperkeratoses, pemphigoid eruptions and herpes were prominent features in their cases. Reynolds[7] and Buchanan[8] have paid particular attention to the nervous phenomena exhibited by a large number of patients during the same epidemic. Polyneuritis was present in a number of them, and it was not infrequently associated with exfoliative dermatitis. Marked muscular atrophy with total paralysis of the affected muscles, especially of the limbs, was frequently observed. Absence of paralysis of the sphincters was a notable feature.

In a number of paretics treated with 0.15 gm. doses of neo-arsphenamin daily, Sicard and his associates[9] ascertained that if a single course of treatment were pursued until a man had received from 8 to 10 gm. and a woman from 6 to 8 gm. bilateral abolition of the Achilles reflex was the rule. The knee jerks were rarely affected. Disappearance of the Achilles reflex was not accompanied by such signs of polyneuritis as difficulty in walking, pain in the limbs or muscular atrophy. This symptom was regarded by Sicard as an important premonitory sign for extreme caution in giving further treatment. He noted that this reflex does not tend to return, at least it has not done so in several patients whom he carefully observed for more than a year. This point is also of importance since in such a case an erroneous diagnosis of tabes dorsalis might readily be made. Patients treated by Sicard with daily doses of from 0.15 to 0.3 gm. of neo-arsphenamin showed tolerance for the drug for some time. As a rule, they did not display evidences of toxemia until toward the end of the second month of treatment, by which time the total dosage would be from 11 to 12 gm. The symptoms observed were principally referable to the skin and its appendages. They consisted of pruritis, erythema, puffiness about the face, trophic nail lesions, loss of hair, plantar keratoderma, abscesses and ulcerations. All of the patients recovered except one, who succumbed to hemorrhages as a result of pharyngeal and postlingual ulcerations. Sicard and Roger [10] also treated a number of paretics with large doses of neo-arsphenamin, giving 1.8 gm. every five days until a total of 10.8 gm. had been reached. All went well until after the sixth, or last, injection when a generalized erythema appeared. Icterus soon became evident, accompanied by gastro-intestinal disturbance and the patients usually sank into a semicomatose state. The urine, normal until then, showed albumin and casts. The other symptoms soon cleared up as a rule, but those affecting the skin and its appendages followed a protracted course resulting in a generalized exfoliation and pigmentation of the body surface. All the hair fell out and the finger and toe nails were cast off. In some instances it required six months for patients to fully recover from the effects of such a course of treatment.

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[6] Brooke, H. G., and Roberts, L.: The Action of Arsenic on the Skin as Observed in the Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Dermat. **13**:121, 1901.

[7] Reynolds: An Account of the Epidemic Outbreak of Arsenical Poisoning Occurring to Beer Drinkers in the North of England and Midland Counties in 1900, Lancet **1**:166 (Jan. 19) 1901.

[8] Buchanan: Cases of Arsenical Peripheral Neuritis, Lancet **1**:170, 1901.

[9] Sicard; Haguenau and Kudelski: Traitement de la syphilis nerveuse chronique. Les elements de controle de la medication novarsenicale, Bull. et mém. Soc. méd. d. hôp. de Par. **35**:833, 1919. Sicard: Traitement des contractures et des etats spasmodiques par les novarsenicaux, pseudo tabes novarsenical, ibid., p. 930.

Sicard and Roger have mentioned a sign of impending arsenical intoxication which is provoked by applying tincture of iodin to the skin of one who is receiving arsphenamin or neo-arsphenamin. If the patient is on the verge of intoxication, they assert that this will speedily produce a vesicular dermatitis at the site of application.

Solomin [11] has reported the occurrence of arsenical polyneuritis in a woman who had received three injections of arsphenamin, 0.3 gm. each, within a week's time. One month later she noticed weakness in both legs associated with hyperesthesia and paresthesia. These symptoms were soon followed by paralysis and muscular atrophy of both lower legs, the extensors being most markedly affected. She recovered after three months.

The case observed by Variot and Bouquier [12] shows the cumulative effect of arsenic in a 13-year-old child who had received three series of injections of arsphenamin, or twenty-one in all. The initial dose in each series was 0.15 gm. and the last one 0.45 gm. An injection had been given every eight days with three weeks repose between series. May 16, 1918, was the date of the last treatment. Early in that same month the patient had complained of pain in the left leg associated with formication. At that time the left foot could be lifted with difficulty. Two weeks later, when first seen by Variot and Bouquier, the right foot and leg were similarly affected and a steppage gait was present. Muscular atrophy of the calf muscles appeared soon afterward. There was no disturbance of sensation. The Achilles reflexes and knee jerks were abolished. The reporters of the case did not discover evidences of any other factor capable of provoking these symptoms and they ascribed them to arsphenamin.

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[10] Sicard and Roger: Arsénothérapie intraveineuse intensive et l'abolition du réflexe Achilléen, Bull. et mém. Soc. méd. d. hôp. de Par. **42**:585, 1918. Sicard and Roger: Intoxication arsénicale chronique après arsénobenzothérapie intraveineuse intensive, ibid., p. 181.

[11] Solomin: More on the Therapeutic Action of 606 and That of 914; Cases of Polyneuritis After the Application of Them Both, Med. Obozr. **79**:587, 1913.

[12] Variot and Bouquier: Polynévrite consécutive à un traitement par l'arsénobenzol, Bull. et mém. Soc. méd. d. hôp. de Par. **42**:783, 1918.

Abadie, Petges and Desqueyroux,[13] as well as Astié,[14] have fully described a case of polyneuritis following a 0.60 gm. dose of arsphenamin. Severe lancinating pains first appeared in the calves and thighs. Later complete paralysis of both arms and legs was noted. The face, trunk and sphincters were not affected. Marked muscular atrophy appeared later. The patient made a slow recovery without further treatment.

Pürkhauer and Mauss [15] have noted the association of Korsakow's psychosis with polyneuritis in a female tabetic who had received two injections of neo-arsphenamin, 0.45 gm. each, one week apart. Two days after the last treatment the patient, who up to this time had apparently been in good physical and mental condition, showed a loss of muscular power in both legs. Her gait became uncertain like that of a drunken person. The affected muscles were painful on pressure. About this time the symptoms of psychosis polyneuritica appeared. She grew steadily worse and died ten days after the last injection.

Bayet [16] has reported a case of multiple neuritis involving both hands and forearms followed by atrophy of the interossei of the thumbs. The patient, a young woman, presenting a macular exanthem had received five injections of neo-arsphenamin, a total dosage of 2.5 gm. within two weeks.

An interesting case of polyneuritis following acute arsenic poisoning has been reported by Raymond and Lejonne.[17] The patient had accidently taken 5 gm. of rat poison containing arsenous acid. Symptoms of polyneuritis appeared three weeks later and involved all of the extremities. The nerve trunks were painful on pressure; the

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13. Abadie; Petges and Desqueyroux: Polynévrite sensitivo-motrice avec troubles psychiques à la suite d'une injection intraveineuse de salvarsan, Ann. de derm. et syph. **4**:17, 1913.

14. Astié: Les complications nerveuses dans le cours du traitement de la syphilis par le 606. Thèse de Bordeaux, 1912.

15. Pürkhauer and Mauss: Ein Fall von Polyneuritis mit Korsakowscher Psychose nach Neosalvarsan mit letalem Ausgang, München. med. Wchnschr. **61**:423, 1914.

16. Bayet: Le néosalvarsan, Presse méd. Belge **64**:755, 1912.

17. Raymond et Lejonne: Polynévrite consécutive à un empoisonment par l'arsénic, Rev. neurol. **14**:79, 1906.

Achilles reflexes were abolished; knee jerks were diminished. Paralysis of the affected parts and later a marked muscular atrophy were salient features.

CASES OF PERIPHERAL NERVE INVOLVEMENT DUE TO SYPHILIS AND MERCURY REPORTED IN THE LITERATURE

Having referred to cases of arsenical polyneuritis, let us discuss briefly instances of peripheral nerve involvement due to syphilis and also mercury.

Most of the cases of true syphilitic polyneuritis, as reported by Fordyce,[18] Fournier,[19] Cestan,[20] Spillmann and Etienne,[21] Raymond, Grosz,[22] Plehn,[23] Gilles de la Tourette, Middleton,[24] Leyden, Trömner,[25] Demanche and Menard,[26] Steinert,[27] and Nonne appeared early in the secondary period, were associated with active lesions of syphilis and responded to specific treatment.

Fordyce's case, which seems to be unique in American literature, may well serve as an example. A man aged 40, presented a macular exanthem and characteristic adenopathy. His chief complaint was inability to walk. The muscles below the knees were tender on deep pressure. Knee jerks were absent. Later distinct atrophy of the leg muscles appeared, affecting especially those below the knees. The bladder and rectum functioned normally. Mercurial treatment effected a quick recovery. Nolda[28] has reported a case of polyneuritis associated with mucous patches of the uvula, soft palate and right tonsil. The nerve trunks of both arms and legs were painful on pressure. Sensation was not disturbed. The symptoms became much worse after a prolonged alcoholic bout and resulted in a complete paralysis of both lower legs. Up to that time the patient had refused mercurial trteatment for fear of being poisoned. A course of mercuric chlorid injections brought about a marked improvement, but there was a relapse after another spree. An example of polyneuritis affecting all four extremities appearing simultaneously with tertiary skin lesions has been observed by Bonnet and Laurent.[29] A primary lesion had been present five years before. Mercury cleared up the lesions in a short time.

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[18] Fordyce: Peripheral Neuritis of Syphilitic Origin, J. Cutan. & Gen.-Urin. Dis. **9**:174, 1891.

[19] Fournier: Traité de la syphilis, Paris, J. Rueff, Editor **1**:663, 1906.

[20] Cestan: Polynévrite syphilitique, Nouv. Iconog. de le Salpétrière **13**: 153, 1900.

[21] Spillmann and Etienne: Polynévrite diffuse dans la periode secondaire de la syphilis, Ann. de derm. et syph. **27**:637, 1906.

[22] Grosz: Neuritis Multiplex in Secunärstadium der Syphilis, Wien. klin. Wchnschr. **10**:572, 1897.

[23] Plehn: Berl. klin. Wchnschr. **42**:1019, 1905.

[24] Middleton: Glasgow M. J. **45**:56, 1896.

[25] Trömner: Nervensyphilis der Frühperiode, Dermatologische Studien. Festschr. f. P. G. Unna **21**:339, 1910.

[26] Demanche et Menard: La polynévrite syphilitique existe-t-elle? Presse méd. **19**:931, 1911.

[27] Steinert: Ueber Polyneuritis Syphilitica, München. med. Wchnschr. **56**: 1938 and 2010, 1909.

[28] Nolda: Neurotabes Alcoholica, oder Syphilitica oder Mercurialis, Neurol. Centralbl. **14**:200, 1895.

The existence of a true mercurial polyneuritis has been much disputed, but nevertheless such cases, though rare, have occurred. Leyden,[30] Spillmann and Etienne,[31] Ketli, Faworski,[32] Brauer,[33] and Petren [34] have made contributions to this subject. The most typical cases, those of Ketli and Faworski, resulted from acute intoxication and did not occur during the course of treatment for syphilis. Ketli's patient swallowed 2 ounces of a 1 per cent. solution of corrosive sublimate, from the first effects of which he apparently recovered. Later symptoms of polyneuritis appeared successively in the feet, legs, hands and arms. Death resulted from asphyxia. In Faworski's case 20 grains of mercuric chlorid were accidently swallowed. Ten days later, after the first effects of the drug had passed away, there was total paralysis of the legs and arms. The extensor muscles were most severely affected, and the nerve trunks were painful on pressure. Recovery ensued, but very slowly. The three patients studied by Spillmann and Etienne presented in addition to multiple neuritis, well marked stomatitis and diarrhea. Two of them were undergoing treatment for syphilis. One of the latter patients had taken 160 yellow mercuric iodid pills each containing ¼ grain of that preparation and had moreover received eleven mercurial inunctions, all within twenty days. The other one, a patient in poor condition, had received six weekly injections of mercury thymol acetate, following which he developed a severe stomatitis and diarrhea and later multiple neuritis of the legs and arms. Severe albuminuria and the presence of mercury in the urine were features in both cases. The patients recovered when the mercury treatments were stopped. The third patient showed no signs of syphilis, but had been treated by a druggist for an acute gonorrheal urethritis and epididymitis. He had been given a mixture for internal use which was found to contain a considerable amount of mercury. Mercurial ointment had been freely applied to the affected testicle for several months and the medicine had been faithfully taken for a like period before untoward symptoms appeared. Petren's case occurred in a syphilitic patient who had received several courses of insoluble mercurial injections. He later showed evidences of polyneuritis and succumbed to what that writer called mercurial poisoning. The necropsy did not help to clear up the etiology.

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[29] Bonnet and Laurent: Polynévrite syphilitique, Ann. de derm. et syph. **1**:433, 1910.

[30] Leyden: Ueber Polyneuritis Mercurialis, Deutsch. med. Wchnschr. **19**: 733, 1893.

[31] Spillmann and Etienne: Polynévrites dans l'intoxication hydrargyrique aigue et subaigue, Rev. de méd. **15**:1009, 1895.

[32] Faworski: Zur Lehre von der acuten Merkuriellen Polyneuritis, Neurol. Centralbl. **19**:377, 1900.

[33] Brauer: Letal endende Polyneuritis bei einem mit Quecksilber behandelten Syphilitischen, Berl. klin. Wchnschr. **13**:14; 1897.

[34] Petren: Sur la question de la polynévrite syphilitique ou mercurielle, observation d'un cas mortel, Nouv. iconog. de la Salpétrière **28**:226, 1916-1917.

REPORT OF A CASE

History.—E. P., a negro, aged 42, was admitted to the Sceleth Hospital, House of Correction, on March 19, 1919. He complained of feeling weak and chilly, but walked in unassisted from the cell house. He denied ever having had syphilis, but admitted having been a heavy whisky drinker for twenty years. Soon after becoming an inmate of the institution his Wassermann reaction had been reported as + +. A careful examination made at that time had failed to reveal any other evidence of syphilis, either hereditary or acquired. Soon thereafter antisyphilitic treatment was begun and carried out as follows: The first course consisted of six weekly intravenous injections of neo-arsphenamin (neodiarsenol brand) given in concentrated solution, as Duhot and Ravaut were the first to suggest. The initial dose was 0.60 gm., subsequently he received 0.90 gm. Besides this, a dozen intramuscular injections of mercuric chlorid (1 per cent. solution) were given. No evidences of intolerance appeared during this time.

After three weeks' rest a second course was begun, since the patient's Wassermann reaction was still positive. He had received two more weekly injections of neo-arsphenamin, 0.90 gm. each, when he suddenly became ill and was admitted to the hospital the day following his last treatment.

Examination.—When admitted his temperature was 99 F., pulse 90 and respiration 20 per minute. A careful examination showed the heart, lungs, abdominal viscera and extremities to be negative. The reflexes were normal. There were no Babinski reflex, tremor or ataxia. The pupils reacted to light and accommodation. A moderate degree of pharyngitis was present.

The patient was a well built man, 6 feet tall and weighed about 175 pounds. He was first seen by the author, March 21. At that time he presented a marked, more or less generalized eruption not unlike a papular urticaria. It was most prominent over the face and anterior surface of the trunk. The lesions were pinhead sized, moderately firm papules which showed no tendency to grouping They were intensely pruritic. The next day his face was greatly swollen, the eyes being almost closed. The skin felt firm and infiltrated and showed evidence of slight scaling, especially about the face, where the papular lesions were less prominent than on the day before. Four days later the entire skin surface was the seat of an extensive exfoliation. At first the scales were small, dry and of a grayish color. Later they were much larger, especially over the hands and feet, finger cot like casts of several fingers and toes being shed. The edema had become more or less generalized, being very evident over the scalp. The skin condition was diagnosed as exfoliative dermatitis at that time.

A blood examination made on March 25 showed the erythrocytes to be almost normal in number, the leukocytes 21,600 per cubic millimeter and hemoglobin 90 per cent. A urinalysis showed the presence of bile pigment as well as a few hyaline and granular casts. Albumin and sugar were not found then or later.

Course and Treatment.—About April 1 a bilateral mucopurulent conjunctivitis appeared and remained for several weeks. The edema was much lessened. The patient by this time was commencing to show emaciation. As a result of industrious scratching, numerous excoriations and foci of superficial infection were present especially over the lower back, flanks, thighs, shoulders and abdomen. Early in that same month bed sores appeared in the sacral region and about both heels. These ultimately became extensive and reached down to the underlying bony structures. The sacral sore attained a diameter of almost 10 cm. During a large part of April the patient was irrational. Dr. Sidney Kuh saw him late in that month and stated that any mental disturbance present was probably of toxemic origin.

Early in May a large abscess appeared below the angle of the left scapula. The exfoliation, though still present, was appreciably diminished. About this time the patient said that he felt sharp pains in his feet and in the lower part of his legs. A little later he exhibited a slight steppage gait. His hands also began to show signs of weakness and it was difficult for him to grasp and retain objects. On May 11, foot and wrist drop appeared, the former being more marked. Beginning in the toes and the fingers, this condition gradually extended upward to the lower part of the legs and to the forearms, although they were affected to a lesser degree than the more distal parts. By this time he could not stand or raise himself up and had to be fed. The Achilles reflexes were almost abolished, but the knee jerks showed only a slight diminution. The affected muscles were tender on pressure. Muscular atrophy appeared soon after the paralysis, coming first in the feet and hands and thence extending centripetally in a like manner. There was no interference with either the rectum or bladder.

Dr. Kuh was kind enough to examine the case again, June 19, with the following result: "Complete paralysis of all muscles below the knees with marked atrophy; paresis and somewhat less marked atrophy of leg muscles above the knees; contractures of both calf and hamstring muscles; tendo Achilles reflex very slight. Knee jerks fairly brisk; adductor reflex present; no impairment of sensation in extremities; loss of muscular grip more marked on left side than on right; some contractures of flexors of upper arms and diffuse paresis of all the muscles of upper extremities; no disturbances of the cranial nerves; pectoralis major and deltoid muscles good."

From these findings the case was regarded as one of polyneuritis. A flaccid paralysis beginning peripherally and extending centripetally, accompanied by muscular atrophy, prodromal pains in the extremities, marked pain in affected parts on pressure, absence of bladder or rectal disturbance, absence of Babinski's sign and lack of pupillary changes would speak in favor of such a diagnosis. Pierre Marie[35] and others contend that such cases are almost

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35. Marie, Pierre: Les polynévrites, Rev. gén. de clin. et de thérap. **32**: 116, 1918.

always accompanied by slight cord and even brain changes, but of course the most marked changes are present in the peripheral nerves.

A fatal termination was looked for on at least three occasions. Symptoms of a marked toxemia such as a high fever were present for almost three months. The fever reached its acme 104 F. on April 2. Then came a short remission and then another siege of fever lasting about two weeks. At that time 103.8 F. was the highest point reached. On April 2, perhaps the most critical day, the pulse was 144 and the respiration 36 per minute There was no fever after July 1. The patient lost all of his hair as well as his nails. Diarrhea was present for a time early in April, but not after the nervous symptoms appeared.

In spite of such a serious illness he has apparently made a perfect recovery. When discharged from the hospital, August 7, 1919, he was thin and weak. When seen about two months later he had gained considerably, although he still exhibited a steppage gait, which has now disappeared. At the present time he has so far recovered as to be able to perform nightly as a cabaret entertainer.

The treatment employed was directed toward supporting his strength, cleansing the skin surface and causing the bed sores to heal. Internally, he received for some time quinin sulphate, as Engman and Mook have suggested in cases of exfoliative dermatitis. Later this was replaced by elixir of iron, quinin and strychnin. Locally, a dusting powder of zinc oxid and talcum was employed. Later when the skin was more or less generally infected prolonged baths in a warm dilute solution of potassium permanganate were of distinct value. The bed sores healed slowly under long daily exposures to sunlight and air.

ETIOLOGY OF CASE

There appears to be no reason to doubt that neo-arsphenamin by virtue of its arsenic content was the chief factor in the case. The symptoms were like those following arsenical intoxication. As Obermiller[36] has said in speaking of paralysis due to these arsenical compounds, when grave toxic symptoms appear only after repeated injections one must think of a cumulative effect of the agent employed. Here the drug acted on one already more or less poisoned by alcohol and syphilis, making it easy for the arsenic to assert its well-known affinity for nervous tissue.

Against syphilis being the determining factor is the fact that cases of multiple neuritis due to that disease are, as has already been stated, almost always observed during the secondary period in association with active skin manifestations. The fact that the patient recovered without further specific treatment would also speak against syphilis. Both syphilis and alcohol, however, were doubtless contributory causes.

It would seem altogether unlikely that the symptoms observed in this patient were the result of mercurial intoxication. If so extensive a condition were due to mercury, we should expect to find stomatitis, more marked evidences of gastro-intestinal disturbances, and probably nephritis with a large amount of albumin in the urine. Another point against mercurial poisoning is that most cases of intoxication after injections of mercury follow the use of the insoluble salts, such as calomel and gray oil, and few are noted after mercuric chlorid, as a perusal of Lasserre's[37] exhaustive paper and Levy Bing's[38] thesis will show.

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[36] Obermiller: Ueber Arsenlähmungen, Berl. klin Wchnschr. **50**:966, 1913.

In closing, I wish to express my thanks to Charles E. Sceleth, Dr. Sidney Kuh and other members of the staff of the House of Correction for aid in the study of this case.

32 North State Street.

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[37] Lasserre: Le passif des injections mercurielles, Ann. de derm. et syph. **9**:215, 289, 655, 707, 1908.

[38] Bing, Levy: Les injections mercurielles intramusculaires dans le traitement de la syphilis, Thése de Par., 1902.

THE PROVOCATIVE PROCEDURES IN THE DIAGNOSIS OF SYPHILIS *

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In June, 1917, Dr. J. H. Stokes and I[1] undertook the study of the effect of a small dose of arsphenamin in provoking a positive Wassermann reaction in previously negative blood serum in 103 cases, paying special attention to the value of the test in the diagnosis of obscure syphilis. I propose to review the results of a second series of 285 cases and of a special group of thirty Wassermann series. The provocation of the Wassermann reaction following an injection of arsphenamin was first suggested by Gennerich[2] in 1910; it was confirmed by Milian,[3] and later advocated as a useful procedure by other syphilographers of note in this country. Craig[4] believes that a normal variation occurs in successive Wassermann tests of the same patient. He does not believe that the fluctuation is due to technical error. Haller,[3] however, in a similar review attributed such fluctuations to technical difficulties and not to any variation in the complement-binding power of the serums.

From our previous review we estimated that apparent provocation of the serum Wassermann reaction occurred in 18 per cent. of the patients subjected to a provocative injection of arsphenamin. We obtained presumptive, though not conclusive, evidence that such a phenomenon as a provocative reaction exists. It seemed probable that variations in the technic and reagents are factors in the result. With reference to its diagnostic worth, we believed that in cases in which the test was most needed it offered the least help. In other words, we found the highest percentage of reversals in the cases showing the

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

[1] Stokes, J. H., and O'Leary, P. A.: The Provocative Wassermann Test in the Clinical Diagnosis of Syphilis, Am. J. Syphilis **1**:629, 1917.

[2] Gennerich: Ueber Syphilisbehandlung mit Ehrlich 606, Berl. klin. Wchnschr. **47**:1735, 1910.

[3] Milian, Quoted in Craig, C. F.: The Results and Interpretation of the Wassermann Test, Am. J. M. Sc. **149**: 1915.

[4] Craig, C. F.: The Results and Interpretation of the Wassermann Test, Am. J. M. Sc. **149**:41, 1915. The Wassermann Test, St. Louis, Mosby, 1918, Chap. III.

[5] Haller, D. A.: Variations in the Strength of Positive Wassermann Reactions in Cases of Untreated Syphilis, J. A. M. A. **66**:882, 1916.

most clinical evidence of syphilis. In view of this relation, we were forced to conclude that the test was inferior both to clinical judgment and to the therapeutic test in the recognition of obscure syphilis.

Our second provocative procedure in contrast with our first was based on a conservative Wassermann test made with one Noguchi antigen,[6] and is probably, therefore, relatively free from the deceptive effects which may be obtained by overcholesterinized antigens. Even with the employment of sensitive antigens in our first series we were compelled to conclude that the provocative test has a value in diagnosis of less than one-third that of the therapeutic test and of clinical judgment. The employment of a conservative technic in the second series, as will be seen, still further reduced its relative value.

The indications for a provocative test as determined by the previous work are not discussed separately, because they have proved to be practically identical with the indication for expert syphilologic examination in general. Suffice it to say, that we believe what we call the provocative test is still a necessary procedure in a complete and thorough examination for syphilis whether the suspicion is aroused by clinical evidence or history.

COMPARISON OF RESULTS OF FIRST AND SECOND SERIES OF TESTS

The ideal provocative Wassermann test, conducted so as to provide for every possibility, is not worth the necessary time, labor or expense. As a practical compromise, the blood of each patient, including the blood drawn just before the intravenous injection of arsphenamin was given, was examined daily for seven days.

At the request of the Section on Dermatology and Syphilology, patients who were undergoing the provocative test were meanwhile subjected to special examinations in various departments of the Clinic for evidence of syphilis. An examination of the spinal fluid was made almost as a routine procedure in this particular series. In the 285 cases studied provocation of the serum Wassermann reaction was obtained in 8 per cent. (twenty-three patients) as contrasted with 18.4 per cent. in the first series. We attribute this discrepancy to the difference between the very sensitive Wassermann technic of the first series, including multiple and cholesterinized antigens, and the conservative technic of the second series.

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[6] The Wassermann technic as done at the clinic under the direction of Dr. A. H. Sanford is a slight modification of the original Noguchi system. In the preparation of the amboceptor, dogs have been used instead of rabbits. Human corpuscles have been sensitized by adding a definite amount of amboceptor to the washed corpuscles and placing the mixture over night in the ice box. The sensitized cells are then titrated against various amounts of 40 per cent. diluted guinea-pig serum. The standard antigen for routine work is an acetone-insoluble fraction of heart extracts.

In the course of the series of tests, it was noted that from time to time a patient in whom a provocative effect was expected, presented a positive Wassermann reaction on the blood drawn immediately before the arsphenamin injection. Such cases are obviously not provocative effects and should be classified under the group of Wassermann series. In order to aid in determining whether or not the provocative procedure had any intrinsic value, this observation was extended by the performance of thirty series of seven Wassermann tests each on as many patients, without any provocative injection. The fact that 30 per cent. of the patients thus examined yielded positive tests in the course of the series furnishes convincing evidence that even though a provocative effect may exist as such, much of the clinical value of the so-called provocative test lies in the series of Wassermann reactions which it calls for rather than in the results of an injection of arsphenamin. A series of seven Wassermann tests appears to afford an excellent means of interpreting the fluctuations of the ordinary Wassermann technic which Craig believes are to be expected. Why the percentage of the positive results in the Wassermann series should have been higher than in the provocative it is difficult to say unless we unconsciously selected for this procedure patients who were more probably syphilitic.

In our previous report, and in fact throughout the literature, are numerous citations of graded increases and decreases of the provocative effect from day to day. In the series here reported only two examples of such gradations were observed. The taking of blood at twenty-four hour intervals is a crude means of detecting such gradations, so that I believe it quite safe to trust a complete and sudden reversal from negative to positive and back again without intermediate gradations. The second series of provocative tests has impressed on us the fact that it is impossible to predict the day on which a provocative or a Wassermann series will reverse from negative to positive. Accordingly, all systems in which blood is drawn on specified days after the injection appeal to us as untrustworthy. We may say, however, that no provocative reversal was secured after the eighth day and the majority of the changes from negative to positive occurred between the second and fifth days, inclusive (60 per cent.). Repeated examples were seen in which subsequent clinical and serologic findings confirmed the significance of a single positive test among six negatives.

In our previous report, the belief was expressed that the provocative effect and the Herxheimer reaction to which it has been compared are not necessarily identical. In the second series I had occasion to note the presence of a positive local Herxheimer reaction in the absence of provocative action on the serum in six cases. This fact I believe entitles the Herxheimer reaction to a separate, though not especially important, place among the diagnostic elements of a provocative procedure and makes it imperative that any patient sustaining a provocative series in the presence of an obvious lesion should be observed daily for signs of local reaction.

The vogue of the provocative as a test for cure has declined decidedly of late owing in part to Pollitzer and Spiegel's[7] effective criticism. In our first provocative series we emphasized this feature in the use of the test and were of the opinion that it was of some assistance in reactivating negative Wassermann reactions. In the second series, forty-three patients were examined for the fact of cure. All of them gave definite histories of desultory treatment and presented no clinical signs of the disease. A positive provocative effect was secured in six cases. While these positive effects are valuable and should be tested for, our results fully confirm Pollitzer and Spiegel's observations that positive Wassermann reactions can be secured months after a completely negative provocative test. We found, further, that in the presence of a completely negative provocative test on the blood we were able to obtain positive evidence of syphilis in the spinal fluid in eight cases.

A negative provocative test by no means excludes syphilis from the diagnosis. We were able to show in our first series and to confirm in the present series that 35 per cent. of the patients from whom negative results were obtained are demonstrably syphilitic on therapeutic test. A provocative procedure can, therefore, never be regarded as a last resort and must be continued to a more nearly complete therapeutic test if clinical judgment, based on the history and special examination, seems to warrant it. Emphasis should be placed on the fact that a single arsphenamin injection in superficial lesions has a decided value as a therapeutic test and that this value properly attaches to the provocative procedure as a diagnostic aid.

CONCLUSIONS

Four years of observation of the provocative procedure have convinced us that the same fundamental principles underlie the interpretation of the Wassermann part of the test which underlie the clinical interpretation of the Wassermann test in every phase of the diagnosis of syphilis. The estimation of the sensitiveness or conservatism of the test, acquaintance with the antigens used, and a knowledge of the temperamental tendency of the serologist and of the methods employed in his laboratories are absolutely essential. I have little doubt that with a hypersensitive technic a series of seven Wassermann tests, with or without a preliminary arsphenamin injection, could become a dangerous instrument for the production of false clinical diagnoses. On the other hand, in a technic of average sensitiveness there is little doubt that the test adds from 10 to 20 per cent. to the acuteness of the ordinary Wassermann test, and does so without a correspondingly increased risk of false positives, as with highly cholesterinized antigens. Our second series of provocative tests has convinced us as firmly as the first that clinical judgment and the intensive therapeutic test have an efficiency as diagnostic aids which is two or three times as great as the provocative procedure per se.

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[7] Pollitzer, S., and Spiegel, L.: The "Provocative" Wassermann Test, Am. J. Syphilis **3**:252, 1919.

SUMMARY

1. The provocative procedure employed by the Section of Dermatology and Syphilology of the Mayo Clinic consists of a single intravenous injection of 3 decigrams of arsphenamin, with a series of seven Wassermann tests made at twenty-four-hour intervals, the first blood being drawn just before the arsphenamin injection, and if indicated, daily observation of the patient.

2. Four factors contribute to the diagnostic worth of the procedure: (a) A true provocative effect on the Wassermann reaction. (b) The advantage of a series of Wassermann tests which strikes the average and assists in the interpretation of the spontaneous or technical variations of the ordinary Wassermann test. (c) An opportunity to observe a focal flare-up in a visible lesion, the "Jarisch-Herxheimer reaction." (d) The beginning of the therapeutic test. About one fourth of the value of the procedure is ascribed to the provocative effect, one-half to the Wassermann series, and the remaining fourth is divided between the Herzheimer reaction and the therapeutic response elicited. The provocative procedure, including the Wassermann series, Herzheimer reaction, and early therapeutic effect, adds about 16 per cent. to the sensitiveness of a conservative Wassermann test in the diagnosis of syphilis.

3. Although I believe that gradations in the strength of the true provocative effect are not essential to a positive result, and although a single positive reaction among a number of negative reactions is usually significant, it must be remembered that the provocative procedure here described is subject to the same margin of error and calls for the same interpretation of serologic methods as the Wassermann reaction itself. False positive tests and persistent negative results in the presence of syphilis may occur as in all Wassermann test technics.

4. The use of hypersensitive antigens in a provocative procedure is to be deprecated, since they increase the risk of false positive results beyond the point justified by the general value of the procedure in diagnosis.

5. A negative provocative test does not establish the fact of cure, but a positive provocative result is of assistance in recognizing an infection which might otherwise have remained concealed.

6. The provocative procedure described is of no value alone, and should be regarded merely as a part of a general syphilologic examination. The procedure, for example, may yield negative results in the presence of positive spinal fluid findings.

7. The provocative procedure is not a substitute for clinical judgment, and should be regarded in doubtful cases merely as the beginning of a therapeutic test.

I wish to acknowledge the assistance of my chief, Dr. John H. Stokes, in the arrangement of this material.

STABILITY OF SILVER STAINS AS APPLIED TO SPIRILLAR ORGANISMS

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The silver stains for smears, so frequently applied in the examination of treponemes and leptospiras, and now practically limited to the method of Fontana-Tribondeau and Holland's modification, present a serious disadvantage on account of their inevitable discoloration, more or less rapid, through the action of physical agents (long exposure to the light) or chemical agents (action of the cedar oil used in the immersion).

In view of the beauty of these methods, their importance in microbioscopic preparations for teaching purposes and their unsurpassed advantages in photomicrography, I shall describe the simple technic with which we have succeeded in stabilizing these dyes.

The method consists simply in submitting the stain to the action of a fixing and toning bath. The solution may be placed on the surface of the slide or the latter, already treated by the method of Fontana-Tribondeau, may be tipped into Borrel bottle filled with the solution. As happens in the case of photographic positives, an intensification of color follows a slight discoloration of the silvered surface, finally acquiring a permanent depth. The slide is then taken out, washed and left to dry.

The foregoing chemical changes no longer permit us to consider the preparation a silver dye. The sodium hyposulphite of the fixative having reacted on the silver chlorid (this is formed through interaction of the chlorin from aurous chlorid and silver nitrate), a double hyposulphite of gold and sodium results which gives the ultimate color to the parasites. If lead salts have been employed instead of gold chlorid, as occurs in the majority of fixing and toning baths, pentathionic acid gives the ultimate tone.

The practical result is that the preparations show the microbes stained dark gray—when the lead salts are employed—or bluish black—with the gold salts—both being stable. In addition, the yellow background of the preparation disappears entirely through the transformation of the silver nitrate into silver chlorid and dissolution of the latter in the hyposulphite.

Photomicrograph 1 was obtained with a preparation of treponemes which had been exposed for two months to daylight. In the control

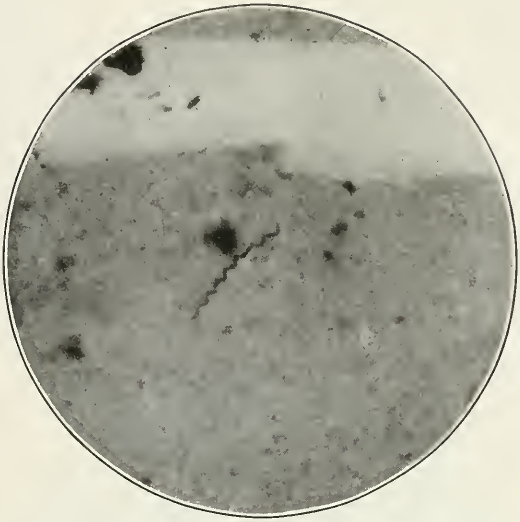

Fig. 1.—Treponeme preparation exposed to daylight for two months after stabilizing.

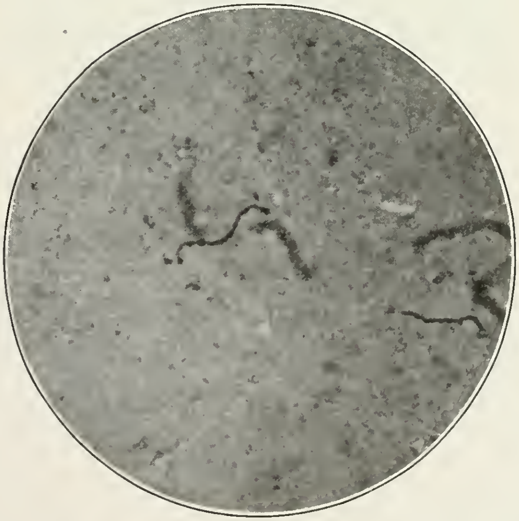

Fig. 2.—*Leptospira icteroides* preparation stabilized two months after being prepared.

preparation, not stabilized according to our method and undergoing the same light action, the treponemas were indistinguishable after three weeks.

Photomicrograph 2 shows a preparation of *Leptospira icteroides* made by Dr. Hideyo Noguchi, Jan. 4, 1920. Two months later the leptospiras could be detected with difficulty. After treating with our technic in a gold fixing bath, we secured a much better staining of the parasites, in addition to a stable color.

The best results are, of course, obtained in preparations stained recently with silver.

As we have indicated, the commercial fixing baths gave good results (the one we employed for the treponemes was manufactured by Burke & James, Chicago). If a black coloring is desired—which may be obtained exclusively through the action of gold and is very stable—one can employ, after fixing in hyposulphite, a toning bath much valued by photographers. This was described by Professor Namias in 1910 before the International Congress of Photography in Brussels, and is of the following composition:

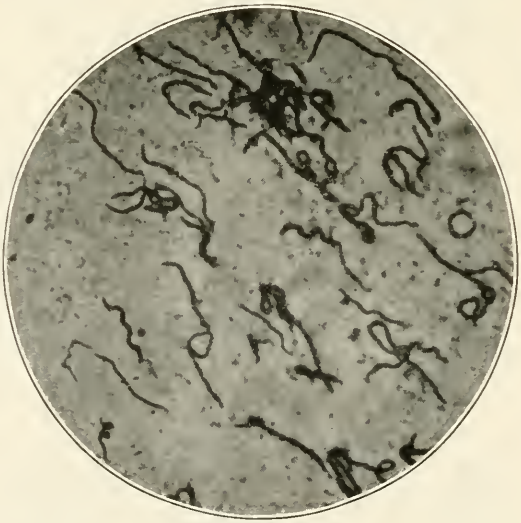

Fig. 3.—Spirillar organisms of Riggs' disease after being stabilized.

	Gm.
Sulphocyanid of ammonium	6.25
Tartaric acid (or citric acid)	0.50
Sodium chlorid	1.25
Water	250.00
Solution of gold chlorid, 1:100	6.25

This formula was employed to stabilize the preparation shown in Photomicrograph 3 (spirillar organisms of Riggs' disease).

Apart from the evident usefulness of this practice of fixing, this technic might suggest other experiments in photographic chemistry, especially in the utilization of platinum, a metal which, as is known, resists powerfully the action of physical and chemical agents. It would also be interesting to apply it to preparations of parasites in the tissues treated with Levaditi-Manouelian's technic, or the most recent one of Warthin and Starry.

A CASE OF LICHEN PLANUS LINEARIS: ITS RELATION TO A CUTANEOUS NERVE EXPERIMENTALLY SHOWN *

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BALTIMORE

Lichen planus occurring in narrow lines, although comparatively rare, has been recognized for a number of years. The condition was known to Cazenave and Devergie as "lichen en ruban" as early as 1843. In most of the cases, since reported, the eruption has apparently followed the course of a cutaneous nerve, especially the small sciatic. Examples of this distribution have been presented to the London Dermatological Society by Crocker, Morris, Pringle and Galloway.

A few cases, however, have been reported in which the eruption followed the courses of other nerves. In one of Mackenzie's cases it followed that of the left ulnar and internal cutaneous nerves and in another it began in the course of some of the intercostal nerves, subsequently becoming general.

More rarely the linear eruption has not apparently followed a nerve, as in Meyer's case in which it was supposed to have followed Voight's lines and in Perry's case in which it corresponded to the course of the long sapheneous vein.[1]

REPORT OF CASE

History.—A carpenter, aged 33, came to the Johns Hopkins Hospital Dispensary in January, 1915. He had had no serious illness and usually enjoyed moderately good health. He did not appear to be of a nervous or excitable nature and had no worries other than those of the average workingman. There was no history of any previous skin disease.

The eruption of which he complained had been present fourteen or fifteen years. It had begun on the back of the right hand and had reached its present dimensions gradually within four or five years. It had practically remained unchanged for the past ten years. Itching was the only subjective symptom and this was not especially marked except when the patient became overheated.

Examination.—The disease was distributed as a narrow band, beginning just above the external condyle of the humerus and extending down over the extensor surface of the forearm and hand ending about the middle of the index finger. The line was practically unbroken and varied in width from 2 to 6 cm. It consisted of discrete or confluent, pinkish or dark red papules from 2 to 5 mm. in diameter. Some of the lesions on the back of the hand were umbilicated and smooth, but most of these on the arm were covered with whitish scales or hemorrhagic crusts as the result of scratching.

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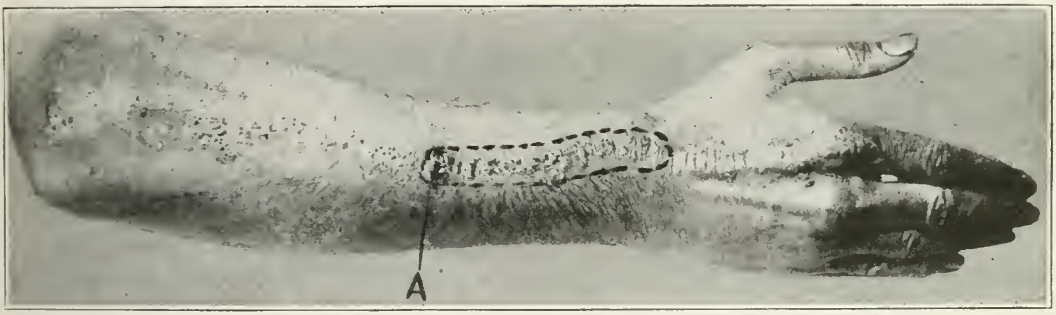
* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22, 1920.

* From the Department of Dermatology, Johns Hopkins University, Medical Dept.

[1] Other cases are reported by Crocker: Brit. J. Dermat. **42**:421, 1900.

The clinical diagnosis of lichen planus linearis was made and substantiated by the histologic examination. The eruption followed the course of the inferior external branch of the musculospiral nerve to its cutaneous end, which is usually at the wrist. Beyond this point it lay on territory supplied by one of the branches of the radial nerve.

Treatment and Course.—Because of the possibility of the disease being dependent on some disturbance in this branch of the musculospiral nerve, it was thought advisable to sever it and note the effect on the eruption. An incision was made through the skin at right angles to the affected line about the middle of its course. It was carried through the subcutaneous tissue beneath which a small nerve trunk about 2 mm. in diameter was found lying on the muscular fascia. This nerve lay directly beneath the eruption and at this point ran parallel to it. The nerve was severed and a small piece removed for histologic examination. (This piece was unfortunately lost during fixation.)



Lichen planus linearis on the arm of author's patient. A, point at which nerve was cut; dotted line encloses approximately the anesthetic area.

The effect of severing the nerve was to produce an area of complete anesthesia to pin pricks which extended 11 cm. below the point of incision and ended just above the level of the lower end of the radius. This anesthetic area followed the course of the eruption and averaged about 3 cm. in width. All of the lesions in this area lay within it. The patient was observed for two or three weeks and then lost sight of for seven months. An examination at the expiration of this time showed that there was no noticeable change in the appearance of the disease and that the area of anesthesia had completely disappeared except over the scar from the incision. He also reported that he had noticed no change in the disease during his absence except the loss of itching over the anesthetic area.

The investigation of this case proves beyond doubt that the eruption of lichen planus followed the course of a cutaneous nerve for about one third of its length, as shown by the co-existence of the anesthetic area and the eruption. It can justifiably be assumed that the remaining portion of the eruption, central to the point of incision, followed the same nerve since it follows the usual course of this nerve and lies within the territory usually supplied by its branches. The portion of the disease over the back of the hand and finger, distal to the lower limit of anesthesia, may have followed the same nerve which has overlapped the usual territory of the radial nerve or a branch of the radial itself. In the former case, protopathic sensibility must have been fully supplied to this area by the radial nerve, or at least, to such an extent that no noticeable diminution of sensation was evident. The work of Head, Rivers and Sherren [2] has shown that there is considerable overlapping and variation of the protopathic nerve fibers and that a very small area of anesthesia, compared to its anatomic distribution, may be caused by severing a cutaneous nerve.

Nothing is known of the nature of the relation of linear lichen planus to cutaneous nerves. It is difficult to conceive that the eruption follows the nerve in the sense that the latter offers an anatomic pathway along which it may be distributed. This would necessarily involve decided sensory disturbances and, furthermore, the inflammatory process of lichen planus is situated much above the usual course of the cutaneous nerve trunks.

Whatever this relation may be it is not possible, in the state of our present knowledge, to support adequately a theoretical possibility, since we know nothing concerning the etiology of the disease itself.

DISCUSSION

Dr. Wise said he always hesitated to make a diagnosis of linear lichen planus unless he saw other lichen planus lesions on the skin or in the mouth. The possibility of nevus linearis occurring in adult life had to be considered. He asked if there was other evidence of lichen planus in this case.

Dr. Ketron, replying to Dr. Wise, stated that there was no evidence of lichen planus on any other portion of the patient's body nor was there any history of it. The histologic picture, however, was typical of lichen planus, showing the round-celled infiltration of the upper portion of the corium and the characteristic epidermal changes.

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[2] Head, Rivers and Sherren: Brain **28**:99, 1905.

A BORDERLINE CASE OF NEUROTIC EXCORIATIONS *

WILLIAM ALLEN PUSEY, M.D.

CHICAGO

MacKee and Senear and I have recently called attention to a group of self-inflicted eruptions, under the title "Neurotic Excoriations." In their slight degrees they are familiar, but the more extreme forms of the condition, while their character is doubtless recognized, have not hitherto been reported in this country. The subject has been described carefully by English authors, notably by Erasmus Wilson, Tilbury Fox, and Adamson. I believe the cases are so frequent that the subject should be impressed on our minds.

The clinical pictures differ from the ordinary feigned eruptions, and the conditions differ essentially from feigned eruptions in the mental states of the patients. In a feigned eruption the patient is secretive and tries to cover up the fact that the eruption is self-produced. In neurotic excoriations the patient has a strong impulse to produce damage to the skin and, while he may not suggest the part that he plays in his injuries, he makes no attempt to conceal it when inquiry is made. His is an entirely different mental attitude from that of the malingerer.

I have recently seen a case in which the amount of destruction of the skin equaled that in many cases of typical malingering, but in this case the psychic condition was that seen in neurotic excoriations. It may perhaps be regarded as a borderline case between the two conditions.

REPORT OF A CASE

History.—Miss X., aged 26, a nurse, who acted as an attendant in a doctor's office, presented herself in December, 1919, with a chronic ulcer of the back of the left hand. There was an atrophic, ulcerating scar extending the full width of the hand, and from the wrist to within a finger's breadth of the knuckles. In the scarred area there were numerous round, crescentic, irregular superficial ulcers. These superficial ulcers were covered with red granulations in which there were numerous islets of growing epithelium. There were other small deeper ulcers, some being in the skin outside the scar, and the whole area was more or less covered with yellowish pus crusts (see figure).

In September, 1918, she burned the left hand with concentrated lye. The burn healed with the formation of a thin scar. The scar was fissured from time to time across the wrist, but the fissures readily healed with zinc oxid ointment. About five weeks before presentation a fissure appeared, but this did not heal on the application of the zinc oxid ointment; the scar began to ulcerate, and the ulceration spread rapidly. Dressings of zinc oxid ointment and other bland ointments, of balsam of Peru, wet dressings of salt solution, hydrogen peroxid solution and the surgical solution of chlorinated soda (Dakin's solution) had been used without avail; the ulcerations continued to spread.

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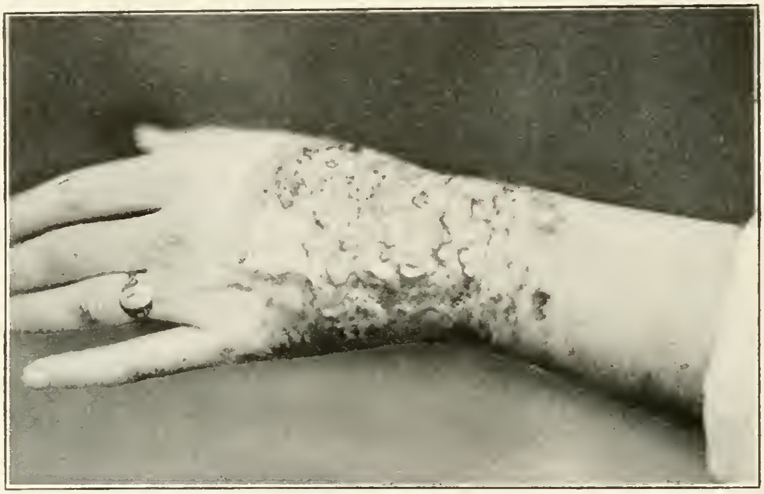
* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

There was nothing significant in the patient's history. Her general health had been good. She slept well. She was an intelligent woman, and her physician employer thought that she was not nervous or high strung, although seven years before, at a time of family difficulties, she showed some tendency to hysteria. Her pharynx and conjunctivae were anesthetic.

The configuration on the back of the hand was not that of the ordinary feigned eruption, but neither did it resemble any known dermatoses. The individual lesions were such as might be produced by local injury combined with simple pus infection. It was not difficult, therefore, to arrive at the conclusion that the injury was probably self-produced. The patient, however, did not present the usual facies of the malingerer. There was not the impassive face, the dejected expression, the downcast eye of the malingering woman. She was alert, looked one in the eye and answered questions without evasion. When the opinion was given that the lesions were self-produced the doctor frankly said he could not believe it. The woman, however, readily admitted that this might be true, as she had found herself constantly picking at the hand, and could not avoid it. She was not secretive or on the defensive. If she was doing it, it was through a nervous impulse which she had not been able to resist, and she was ready to cooperate with us in meeting the situation.



Neurotic excoriation on hand.

Treatment and Course.—I advised the application of weak aluminum acetate solution compresses and an occlusive dressing that would prevent her from getting at the hand. Two and a half weeks later her physician employer wrote me that the hand had healed completely in about a week, but in order to prevent her from irritating the hand at night, she had had to put a muff on her other hand, and for a while it had been necessary for a nurse to watch her at night. It was at night, during her sleep, that she did most of the damage. Her physician, to whom I said nothing about neurotic excoriations of the skin, suggested in his letter that he thought she had not been producing this injury deliberately, but through nervousness, comparing the condition very aptly to biting of the fingernails. After a week and a half of treatment she needed dressings only during sleep, and was able to go on with her nursing as usual.

DISCUSSION

Dr. Schamberg thought Dr. Pusey did well to emphasize the distinction between the two types of factitious dermatitis which were very different in their nature and the motive which prompted them. The feigned eruptions that had as their motive a desire for morbid sympathy or escape from some unpleasant duty, were familiar as were also the so-called neurotic excoriations in which the underlying cause is an uncontrollable and vicious habit, often acquired more or less subconsciously in an effort to aid in the cure of the lesions. He had seen a number of cases of acne in which the patients had produced indelible scars on the face. The patients freely admitted their part in the production of the lesions of the face, but said the lesions would not heal until they were opened. The two types of factitious lesions were very different in their inception. Dr. Schamberg thought that one should also differentiate between neuropathic lesions of the skin of organic origin and those considered above. He recalled a patient who had been for many years under the care of Dr. Duhring whose hand was mutilated by a gangrenous process until it looked like a claw. Pathologic studies of the nerves in the amputated member were made by Professor Spiller of the University of Pennsylvania. Degenerative changes were found which were regarded as primary, but it was impossible to exclude secondary nerve change. He believed three conditions should be considered: the feigned eruptions, the neurotic excoriations and certain neuropathic changes which were due to nerve lesions.

Dr. Ormsby stated that some years ago he had recorded the cases of thirty-four patients who had produced lesions on themselves, and he had seen a number of similar instances since that time. The question frequently arose as to whether these were self-inflicted or were of spontaneous origin. He believed the major portion were self-induced. He had seen none that were spontaneous, and he was therefore interested to hear Dr. Schamberg's report of a proved spontaneous gangrene—Dr. Corlett and a few others had described similar instances. The group of patients recorded by Drs. Pusey and MacKee, while having self-induced lesions, belonged to a different category, but that some of them may be similar was well illustrated in the case reported by Dr. Pusey. Had this patient been seen some years ago it probably would have been considered an example of feigned dermatitis. The history, together with the lesions in the light of our present knowledge, removed it from that group and properly placed it with neurotic excoriations.

Dr. Engman believed that the sexual element was important in these cases. Some years ago he and Dr. Schwab reported a case in which there was a decided sexual element. The young woman had, when picking her skin, a distinct sexual feeling. In the case of acne excoriation there was such a history, and it was an important fact in analyzing these cases to go into the sexual history. Sometimes, in the freudian sense, it was the basis of the trouble and these patients obtained some sexual gratification in picking the skin.

Dr. Hazen said that he had seen a pruritus of the genitals develop when patients were unhappily married and also when they had failed to be married when they expected to, and he thought most cases of pruritus vulvae would fall into the same group. He believed that psychanalysis would be valuable in these cases, if it were possible to get a good man to cooperate.

Dr. Pusey (closing) said that he was familiar with the sexual element that complicated many cases of feigned eruption, but he was not inclined to think that this was an element that was apt to be encountered in neurotic excoriation. The impelling fact in these cases was the nervous impulse to pick at a lesion, and he was anti-freudian enough to believe that this impulse could reasonably be thought in most cases not to have a sexual element. He was particularly interested in the sharp mental distinction between the patient in the case he had just reported and the malingerers. He tried to bring out the contrast in the report. He had never seen a malingerer whose attitude had been the frank one of this patient.

PROTEIN SENSITIZATION IN ECZEMA

REPORT OF SEVENTY-EIGHT CASES

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In reporting this series of cases, I especially wish to call attention to a particular phase of the clinical applicability of protein sensitization which is commanding wide interest and gaining rapidly in importance. Our present knowledge of the etiology and specific treatment of eczema is so vague, that any procedure indicating a clearer understanding of this condition is indeed worthy of special note.

In reviewing the literature on this subject, one is impressed by the variance of opinion, and results obtained. Blackfan,[1] using both the cutaneous and the intradermal method of testing, obtained a positive reaction to proteins in twenty-two of twenty-seven patients with eczema; Strickler and Goldberg[2] obtained positive reactions in six of thirteen cases tested, but these observers used only fourteen proteins and did not consider a reaction as positive unless it persisted for forty-eight hours, thus lowering the percentage of positive cases; White,[3] using proteins, butter, lactose, etc., concludes that 80 per cent. of the cases of chronic eczema are due to food sensitization. During the past few years numerous reports on the relation of anaphylaxis to eczema have appeared in the literature, but there seems to be no uniformity; I believe this is in great part due to differences in technic and standards of positive reaction.

In the following table I have not attempted to include the various metabolic studies which are necessary in the proper study of eczematous patients, but am merely submitting a record of protein skin tests in a series of eczema cases.

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1. Blackfan, K. D.: Cutaneous Reaction from Proteins in Eczema, Am. J. Dis. Child. **11**:441, 1916.

2. Strickler, A., and Goldberg, J. M.: Anaphylactic Food Reactions in Dermatology, J. A. M. A. **66**:249 (Jan. 22) 1916.

3. White, C. J.: Eczema, J. Cutan. Dis. **34**:57 (Feb.) 1916; Ibid., Boston M. & S. J. **178**:5 (Jan. 3) 1918; Ibid.: Two Modern Methods to Be Employed in the Treatment of Chronic Eczema, J. A. M. A. **68**:81 (Jan. 13) 1917.

Results of Protein Skin Tests

PATIENTS TESTED

	No. Cases
Males	52
Females	26
Under 1 year	2
Between 1 and 10	10
Between 10 and 20	8
Between 20 and 30	37
Between 30 and 40	14
Above 40	7
Total	78

PATIENTS GIVING A POSITIVE PROTEIN SKIN TEST

	No. Cases
Under 1	2
Between 1 and 10	8
Between 10 and 20	4
Between 20 and 30	12
Between 30 and 40	3
Over 40	1
Total	30

PATIENTS WITH ECZEMA ASSOCIATED WITH BRONCHIAL ASTHMA

	No. Cases
Under 1	2
Between 1 and 10	6
Between 10 and 20	2
Between 20 and 30	4
Between 30 and 40	0
Over 40	0
Total	14

PATIENTS WITH ECZEMA ASSOCIATED WITH HAY FEVER

	No. Cases
Under 1	0
Between 1 and 10	1
Between 10 and 20	1
Between 20 and 30	0
Between 30 and 40	0
Over 40	0
Total	2

ECZEMA ASSOCIATED WITH BOTH ASTHMA AND HAY FEVER

Occurring between the ages of 1 and 10.................................. 1

DURATION OF THE ECZEMA

	No. Cases
Less than one month	14
One to six months	45
One to two years	11
More than two years	8
Total	78

DISTRIBUTION

	No. Cases
One hand	40
Both hands	26
Both arms and feet	4
Face	6
Entire body	2
Total	78

RESULTS

	No. Cases
Cured	10
Improved	12
Not improved	8
Total	30

POSITIVE REACTION TO VARIOUS PROTEINS

	No. Cases
Milk (cow's)	4
Egg white	14
Whole wheat	2
Corn	7
Rice	4
Rye	2
Oats	3
Pork	3
Potato	4
Lettuce	3
Celery	8
Cabbage	2
Herring	1
Lobster	1
Crabs	1
Veal	2
Beef	3
Ragweed	4
Timothy	2
Total	70

Total number of cases reacting to a single protein	3
Cases showing multiple sensitization	27
Total	30

TREATMENT

The treatment of these patients consisted solely in the removal of the protein giving a positive reaction from the diet. The skin scarification method was used, and reactions were called positive only when a definite wheal measuring 0.5 cm. in diameter appeared. In the cured and improved cases, the improvement was noticed within the first week. In the apparently cured cases there has been no recurrence within six months, and in some cases one year, though they are taking small quantities daily of the foods to which they were originally sensitive. Skin tests performed six months later in six of the cured cases, gave negative results.

SUMMARY

Of seventy-eight cases of eczema tested with proteins, thirty gave positive skin tests. Like asthma, anaphylactic eczema occurs more frequently under the age of 30. Eczema associated with asthma or hay fever is usually anaphylactic. Only a small percentage of all eczema cases are anaphylactic, but it is essential that patients be thoroughly tested in order that they may be properly classified and treated.[4]

2 West Eighty-Eighth Street.

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[4] In addition to the references already given, the following will be found of interest:

Talbot, F. B.: Med. Clin. N. America **1**:985 (Jan.) 1918.

Walker, I. C.: Causation of Eczema, Urticaria and Angioneurotic Edema, J. A. M. A. **70**:897 (March 30) 1918.

Fordyce, J. A.: J. Cutan. Dis. **29**:129, 1911.

McBride, W. L., and Schorer, L. H.: J. Cutan. Dis. **34**:70 (Feb.) 1916.

Hoobler, B. R.: Tr. Am. Ped. Soc. **28**:188, 1916.

Schloss, O. M.: A Case of Allergy to Common Foods, Am. J. Dis. Child. **6**:341 (June) 1912; Tr. Am. Ped. Soc. **27**:62, 1915.

Haller, D. A., and Walker, I. C.: Syphilis with Neurologic Symptoms Simulating Other Conditions, J. A. M. A. **67**:1497 (Nov. 18) 1916.

Fisher, L.: New York M. J. **108**: 804 (Nov. 9) 1918.

ADENOMA SEBACEUM ASSOCIATED WITH A TERATOMA OF THE KIDNEY

REPORT OF A CASE *

E. D. CRUTCHFIELD, A.B., M.D.
GALVESTON, TEXAS

The occasional reference in literature to adenoma sebaceum associated with congenital tumors of the kidney or other abdominal viscera leads me to report this case of adenoma sebaceum with an associated teratoma of the kidney.

H. Goldenberg[1] has recently called attention to the frequence of adenoma sebaceum and various congenital tumors. Rosen and Wolf[2] have recently presented a case of adenoma sebaceum in a boy, aged 11, in which a history of the removal of a tumor of the kidney of the Wilm type was obtained. Lapowski[3] has referred to a case of adenoma sebaceum and peculiar tumors of the heart and kidney — not sarcomas—in the *Annales de Dermatologie et Syphiligraphie,* 1914-1915.

REPORT OF A CASE

History.—Stella J., a Caucasian woman, an American, aged 27, the mother of two normal children, whose mother and sister were living and well, and whose father and brother had committed suicide, presented numerous small, pinhead to split-pea sized nodular growths on each side of the nose, cheeks and forehead. The tumors were somewhat symmetrically placed and piled up in the nasolabial folds. The color varied from brown to red. She had marked associated telangiectasia and large coarse pored skin. The patient was mentally alert and of normal intelligence. She was unable to state when the lesions first appeared, but was sure they became more pronounced about puberty. Diagnosis: Adenoma sebaceum. Three weeks later she presented herself in the surgical service of Dr. A. O. Singleton with a temperature of 104 F., pulse 116, complaining of continuous pain in her left side, sweats, nausea and vomiting.

Examination.—The blood showed leukocytosis. The urine from the right ureter contained a little albumin and a few leukocytes; the urine from the left ureter contained much blood. Roentgen-ray examination showed the left ureter displaced toward midline. Examination revealed a tumor mass from the costal margin to the brim of the pelvis and extending to the midline anteriorly.

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* From the Department of Dermatology and Syphilology, University of Texas.

1. Goldenberg, H., in discussion on Rosen and Wolf: Adenoma Sebaceum, Arch. Dermat. & Syph. **1**:329 (May) 1920.

2. Rosen and Wolf: Adenoma Sebaceum, Arch. Dermat. & Syph. **1**:329 (May) 1920.

3. Lapowski, B, in discussion on Rosen and Wolf: Adenoma Sebaceum, Arch. Dermat. & Syph. **1**:329 (May) 1920.

Necropsy Examination.—At necropsy a tumor of the left kidney was found strongly adherent to the diaphragm and lumbar muscles. Many vascular adhesions passed from the capsule of the tumor in all directions. The right kidney was also about four times its normal size and of about the same consistency as the tumor mass and strongly adherent posteriorly. Grossly, the tumor was twice the size of a child's head and of a doughy consistency. Microscopically, Dr. Henry Hartman found the tumor to consist of smooth muscle, fat and larger areas of sarcoma and reported the tumor a teratoma of kidney (Wilm type).

I am indebted to Dr. A. O. Singleton for the privilege of reporting these findings.

ERRATUM

In the August issue of the Archives of Dermatology and Syphilology the paragraphs beginning with "Dr. G. H. Fox," the third line from the top on page 262 and extending to the next case report "Melanoma Treated by Radium," should have followed the case report on "Dermatitis Herpetiformis" on page 264.

Editorial

TEACHING THE UNKNOWN

I once heard a philosopher say that "much time is wasted in learning what is not so." It has often occurred to me that this trite homily applies with special force to the teaching of dermatology. Who that has taught dermatology for many years but can recall many precious hours wasted in teaching what is unknown? This carries with it a double loss, for in addition to the loss of time to the teacher, the student is supposed to memorize much that is only of doubtful value, and dogmatic assertions concerning the unknown tend to unfit him for helpful individual inquiry.

The lack of exact knowledge of disease of the skin by the average family doctor is almost appalling. In speaking of this to a graduate of one of the foremost universities of this country, whose teacher was one of the Nestors of American dermatology, he openly admitted that while he had attended ————'s lectures and passed his examinations, still he knew nothing about dermatology. This confession from one of the most successful practitioners, himself a teacher of medicine, is a subject deserving of thought. One reason why dermatology is not a *pons asinorum* to medical students is that diseases of the skin were among the first to receive attention and much of the nomenclature of today goes back to the time of Hippocrates and to the reign of Darius II, king of Egypt. For two thousand years, therefore, they have been the objects of study, of painstaking observation and of record. What surprises us is that this accumulated knowledge does not give us a clearer insight as to the cause and cure of some of the diseases of the skin whose names indicate that they were known long before the circulation of the blood was discovered by Harvey and while epilepsy was considered to be due to the harboring in the body of "evil spirits." At the same time, I believe that the progress made and what is actually known in dermatology will compare favorably with that in other departments of medicine.

Another reason why the family doctor does not do justice to the patient with a disease of the skin, is that the subject of dermatology as taught in our leading medical schools is an exceedingly complex theme whose very nomenclature constitutes almost a language in itself.

To teach dermatology successfully so that the future medical man may have some definite knowledge of cutaneous manifestations and their significance and be able better to give relief or at least not to harm the patient and to know his own limitations, the subject should be simplified and everything culled from it that the student has not time or inclination to master. Limit instructions, therefore, to the common things, the nature of which we are reasonably sure, and leave the bulk of dermatologic lore to be acquired by one who seeks advanced standing or aims to specialize in this subject.

In addition to this, I would strongly emphasize the importance of not teaching "what is not so." Recently I heard of a whole lecture given up to parapsoriasis to a class of third year students. It is better to endeavor to stamp on the mind the clinical picture of plain, well defined psoriasis and that we know nothing as to its cause and little of its amelioration and cure.

The teacher should bear this in mind and not confuse a receptive mind with doubtful or unknown things. Pemphigus may be cited as another example, because this venerable disease is now denied even an existence by some, and to all its cause and cure are as little known as when Galen called attention to its uncertain position in dermatologic nosology and Sauvages finally stamped it with his approval as a disease *sui generis,* as it is generally understood today. If the teacher is successful in the allotted time of most curriculums in impressing the student with simple, easily applicable and indubitable facts—leaving the doubtful legion of unknown things for them to unravel at some future time, he will accomplish all that our present knowledge vouchsafes, and in addition if his precepts and example have stimulated in his students the desire to seek the truth and to unravel some of the knotted skeins that the eye sees without understanding, he will have accomplished all that a successful teacher is supposed to attain.

W. T. C.

Abstracts from Current Literature

SOME OBSERVATIONS ON SYPHILIS OF THE CENTRAL NERVOUS SYSTEM. G. O. Scott and G. H. J. Pearson, Am. J. Syphilis **4**:201 (April) 1920.

The authors discuss the incidence, etiology, and type of syphilis of the nervous system. Special attention is given to the significance of the different laboratory findings and the associated clinical evidence. They report a series of 210 cases, which they classify according to the variations in the different laboratory findings.

They conclude:

1. The *Spirochaeta pallida* invade the central nervous system during the early part of the stage of generalization of syphilis.

2. On account of the great damage done by the *Spirochaeta pallida* to the central nervous system, if treatment of a neurosyphilitic is delayed, a proper diagnosis should be made and treatment instituted at the earliest possible date, namely, before clinical signs appear.

3. The only certain method of making this diagnosis when it will be of most value to the patient is by performing a lumbar puncture and examining the cerebrospinal fluid A lumbar puncture should be made on every patient with generalized, late and asymptomatic syphilis, on every patient with primary syphilis with a positive blood Wassermann reaction and on every patient with nervous disease. There is no reason why a lumbar puncture cannot be made in ordinary office practice.

4. If the serology does not indicate the presence of the *Spirochaeta pallida*, they do not advise treatment directed with special attention to the nervous system. They do not consider that the following findings in the cerebrospinal fluid indicate an invasion of the *Spirochaeta pallida* in an early case of syphilis without nerologic signs:

(*a*) Cells 0 to 7; globulin not increased; Wassermann reaction negative; colloidal gold curve, negative.

(*b*) Cells 0 to 7; globulin increased; Wassermann reaction negative; colloidal gold curve negative.

(*c*) Cells 0 to 7; globulin normal or increased; Wassermann reaction positive; colloidal gold curve, negative.

These cases should be watched with the greatest of care, but unless further indications appear at a later date, no other treatment than systemic is necessary.

5. If the serology indicates invasion of the central nervous system by the *Spirochaeta pallida*, they advise special treatment for the condition of the nervous system. They consider that the following serology findings indicate neurosyphilis, even though clinical neurologic findings are negative:

(*a*) Cells increased over 7; globulin not increased; Wassermann reaction negative; colloidal gold curve, negative.

(*b*) Cells increased over 7; globulin increased; Wassermann reaction negative; colloidal gold curve, negative.

(*c*) Cells increased; globulin normal or increased; Wassermann reaction positive; colloidal gold curve, negative or positive.

6. All patients with generalized, late or asymptomatic syphilis should be given a neurologic examination, for in a few cases of late degenerative neurosyphilis the clinical findings are positive, but serologic findings are negative. Neurologic findings are a guide to the treatment to be adopted.

7. If the stage of invasion by the *Spirochaeta pallida* is early, systemic treatment may be all that is necessary. If the stage of invasion is later or if neurologic signs are present, combined systemic and intraspinal treatments are a necessity.

8. Ogilvie's modification of the Swift-Ellis method is the most advantageous for the preparation of arsphenamized serum. There is no reason why intraspinal treatment cannot be given in ordinary office practice.

9. In cases of tabes with marked clinical signs, caution should be used in commencing intraspinal treatment on account of dangerous precipitation of symptoms.

Tomlinson, Omaha.

PRENATAL SYPHILIS. John A. Kolmer, Am. J. Dis. Child. **19**:344 (May) 1920.

The author makes a strong plea for the study and prevention of the disease in the prenatal period, and urges cooperation between dermatologists, pediatricians and obstetricians in the care and management of these cases before and after birth. Probably most can be done toward checking the spread of syphilis, and particularly its transmission to offspring, by subjecting prospective and potential parents to clinical, and especially immunologic, examinations for syphilis, and affording adequate treatment within the means of all, including the poorest of persons, seeking medical aid in our dispensaries.

It has been stated that a man ceases to be infectious within from two to five years after contracting syphilis, depending on the thoroughness of treatment, but that a woman may transmit the disease for an indefinite period; this is probably fallacious teaching in so far as the infectiousness of men is concerned. Fournier, for example, in a study of 142 men who contracted syphilis prior to marriage and infected their wives, found that twenty-eight, or about 20 per cent., were known to have been syphilitic for from five and one-half to eighteen years.

Kolmer believes that it is proper to regard all children as probably syphilitic when born of parents one or both of whom react positively to the Wassermann test, even though both the child and parents are clinically free of the disease. Congenital syphilis may manifest itself in so many different ways that the usual clinical picture carried in the minds of the majority of physicians, namely, the child presenting the appearance of "the little old man with a cold in the head" and blebs on the skin, serves for the clinical diagnosis of but a small percentage. As is well known, there may be no discernible lesions and symptoms, and all immunologic tests, such as the Wassermann and luetin tests, may be negative because so many prenatal infections are with treponemas of attenuated virulence inducing activity for several years after birth. As all evidence indicates that a persistently positive Wassermann reaction means presence of living treponemas in the body even in the absence of discernible lesions and symptoms, and since the possibility of transmission of these to offspring always exists, particularly from the mother with a positive Wassermann reaction, the author believes that the physician does well to regard with suspicion the offspring of such parents and even to institute specific treatment as a precautionary measure, especially if such children are manifestly below par in weight and nutrition.

Congenital syphilis should draw both obstetrician and pediatrist into closer professional cooperation, and constitutes an important reason for enlisting the services of the pediatrist in the care of the child before its birth instead of some weeks or months after. The obstetrician alone, and the prenatal clinic, by adequate treatment of the unfortunate parents, can do most in lowering the high but really unknown percentage of intra-uterine deaths of human beings who never had a chance for survival. The pediatrician can aid in this work if he is called in time and given an opportunity, and he may do much toward lowering infant mortality by bearing in mind the wide dissemination of syphilis among persons of marriageable age in both sexes, and the imminent danger of transmission to their offspring.

Waugh, Chicago.

A VALUABLE METHOD OF EMPLOYING ARSPHENAMIN IN SYPHILIS. Oliver S. Ormsby. J. A. M. A. **75**:1 (July 3) 1920.

The author describes a modification of the so-called Pollitzer method of administering arsphenamin. In the early stage, before generalization has occurred three injections of arsphenamin are given with an interval of one day between the injections. The average dose is 0.4 gm., but in some instances 0.5 or 0.6 gm. are given if the patient is large and vigorous. In patients not previously treated the first dose is never more than 0.2 gm. Following this, one month's treatment with mercury, either by injection or inunction, is employed. Six weeks from the last arsphenamin injection, three more are given. In well developed cases not previously treated, the same procedure is employed, except that after the second series of arsphenamin twelve injections of mercuric salicylate are given at weekly intervals, or their equivalent in inunctions over a period of three months, when a third series of arsphenamin is given as before, this being followed by another three months of mercury. In the second year two series of treatment are given in the Wassermann negative cases as a prophylactic measure. In the Wassermann positive cases the procedure is as outlined for the first year.

Ormsby states that the method of treatment described in this communication proved efficient in a number of cases resistant to other methods. The absence of untoward results and reactions of any moment in the large number treated makes it appear as safe as other methods. It seems evident from experimental work herein reported that frequently repeated small doses, that is, from 0.1 to 0.15 gm., are inefficient. The combined use of arsphenamin and hydrargyrum in periods, either as herein described, or by the method commonly employed today in which arsphenamin is administered every five or seven days in series of from five to eight injections, appears at present to be the method of choice. The promptness with which many patients become clinically free and Wassermann negative, often after a single course, is encouraging, but should not lead to the conclusion that the disease is eradicated, as Wassermann relapses occur from six months to a year or more after continuous negative reactions have been obtained. It is therefore necessary to continue treatment for from one to two years, even though it may seem superfluous in some cases.

Waugh, Chicago.

PELLAGRA IN EGYPT DURING THE WAR, COMMITTEE REPORT.

London Letter, J. A. M. A. **74**:1658 (June 12) 1920.

In 1918, owing to the presence in Egypt of a large number of prisoners of war suffering from pellagra, a committee was appointed to investigate the situation. It was found that the deficiency disease in this instance was due to insufficient assimilation of protein. The disease is characterized by erythema and pigmentation of the exposed parts of the body, on the back of the hands first, a fortnight later on the feet, these discolored patches being dry and not sweating even under pilocarpin administration. Profound disturbance of nutrition with early wasting of the muscles of the shoulder girdle, and progressively increasing fall of blood pressure follow. Loss of appetite is a very early symptom, and there is defective secretion of hydrochloric acid in the gastric juice. Herewith there is impairment of digestion, both gastric and pancreatic, malassimilation of protein and fat, and an increased bacterial growth in the intestines, with intermittent diarrhea leading to further loss of ingested, but incompletely absorbed, food. The enhanced destruction of protein gives very foul smelling stools and indican appears in the urine in increasing quantities; apathy comes on, perhaps melancholia, and the patient dies. Death is due to some intercurrent infection: pneumonia, dysentery. tuberculosis, and malaria accounted for 91 per cent. of deaths.

The important question was how this disease was to be prevented. Eighty-eight per cent. of the cases arose among newly captured Turkish prisoners, who for months had available only two thirds of their normal rations, and had suffered "from long continued undernutrition," as their German general had reported the year before. Further, the protein of their diet came mostly from wheat, barley or maize. very little from meat. Now Hopkins and Wilcox, in 1907, showed that the chief protein of maize cannot keep rats alive, as it does not contain enough tryptophan, an amino-acid of the aromatic series; in 1913, Sandwith suggested that want of tryptophan might help to cause pellagra. The committee had the help of Prof. W. H. Wilson of the Cairo School of Medicine, who has long been working at the different nutritional values of the proteins, which seem in part to depend on their individual amino-acids. For the making of epinephrin a benzene nucleus is essential. For the production of this the human organism depends on the hydrolysis of special proteins in the food supply, and even then the yield of tryptophan in this process may be broken up by an overwhelming bacterial flora in the duodenum. Every diet scale considers how much protein is necessary for the man of 70 kg., which is agreed to be 40 gm. daily. But that means grams absorbed, and for normal persons must be increased by one tenth; but experiment proved that for Turkish prisoners it required to be increased by one half, so that, even if they had received full rations, the Turks would have been underfed. But, further, they were fed on the wrong proteins. Wilson calculated the "biologic value of the proteins" (B. V. P.) of various foodstuffs, and found that, to replace 30 gm. of meat as protein supply in a man's diet, 34 gm. of rice protein were necessary, 50 of beans, 76 of bread, and 102 maize. Maize-eating people, therefore, suffer from pellagra because it has the lowest biologic value of the proteins of all the cereals, and if damaged or decayed it is all the less nutritious and pellagra arises more quickly. Vegetable proteins are not so easily assimilated as those in meat, and, further, the beans for the prisoners were not at first well cooked. These difficulties were all adjusted, but it was found that men might escape pellagra on a particular diet while resting, but succumbed as soon as they worked hard; so the diet for heavy labor, though showing already sufficient calory value and vitamin content, had to be increased; then the pellagra ceased.

Waugh, Chicago.

A STUDY OF FOUR CASES OF BEGINNING SQUAMOUS-CELL CARCINOMA OF CORNIFYING TYPE. R. C. Whitman, J. Cancer Res. **5**:155 (April) 1920.

The lesions investigated appeared in verrucous keratoses and showed microscopically pearl formation and cells typically large and round with vesicular nuclei and abundant, opaque protoplasm. Associated degenerative changes in the corium were elacin, basophilic collagen and leukocytic infiltrate invading the cutis. The latter changes are frequently encountered in this type of carcinoma and are characteristic of senile skin.

Case 1.—The patient had a cornifying carcinoma arising multicentrically from the basal and prickle cell layers of the epidermis and hair follicle with early stages of growth within the margins of the verruca not in themselves appearing malignant. The usual associated inflammatory reaction was absent.

Case 2.—This patient presented a cornifying carcinoma arising diffusely from the germinal layer of the epidermis, characterized by "blue areas" of degenerated collagen, elacin degeneration of deep lying elastic tissue, inflammatory changes of contiguous corium, as shown by dense deep cellular infiltration and vascular changes and, among the epithelial features, a bud of proliferating epithelium apparently arising from the basal layer and hair follicles and presenting a disorderly arrangement of large spindle-shaped cells with large pale vesicular nuclei containing deep staining nucleoli.

Case 3.—A cornifying carcinoma arising diffusely from the basal layer only and presenting on section interruption and degeneration of basement membrane, basophilic collagen invaded by acanthotic epithelial pegs, absence of wandering cells, changes in the basal layer represented by intensification of staining and enlargement of individual cells, ramifying and proliferative growth and formation of numerous small epithelial pearls and keratinized channels of epithelial structure surrounding blood and lymph vessels.

Case 4.—This patient presented a cornifying carcinoma arising diffusely from the prickle cell layer only in which the malignant growth was within an intact basal layer which in places surrounded the proliferating cells in a glandlike arrangement. The epidermis showed acanthosis, abundant mitoses confined to the prickle cells, atypical cellular growth and formation of malignant buds. The corium showed elacin, basophilic collagen, eosinophilic infiltrate and a vacuolated hyaline coagulum in places replacing the basement membrane.

In a discussion of theoretical considerations the writer upholds the hypothesis that the cancer cell is a mutated somatic cell and shows the impossibility of a tumor being produced through the reversion of a mature cell to an embryonic stage of development.

The preceding study of the four cases of carcinoma of the same general type, no two of which are exactly alike in the details of origin and growth, is regarded not as a reason for assuming the result of adaptation to differences of environment, but for believing that the differences of behavior are proof of corresponding differences in the inner structure and life of the cell.

The tumor cell is defined as a cell arising by mutation from a normal somatic cell existing normally in the tissues, or displaced as a cell rest, and usually retaining enough of the properties of the parent cell to render its point of origin recognizable. Mutative changes are thought to be favored by hybridization and mongrelization and brought about by such chronic irritations as excite, over a long period, constantly renewed and constantly defeated efforts at repair.

Recurring mutations in a growing tumor bring about a progressive loss of the original character of the mother cell, explaining the lack of uniformity in the biologic properties of a carcinoma and the difficulty in recognizing histologically the real beginning of a carcinomatous process.

H. R. Foerster, Milwaukee.

TOXIC JAUNDICE IN PATIENTS UNDER ANTISYYPHILITIC TREATMENT. C. V. Bailey and A. MacKay, Arch. Int. Med. **25**:628 (June) 1920.

It cannot be recognized before treatment which patients are susceptible to arsenic toxemia, either early or late, although urinary examinations should always be made previous to the use of arsphenamin.

The writers examined the blood and urine in twenty-five cases of toxic jaundice following antisyphilitic treatment, and in fifteen cases of other diseases. The toxic period had varied from sixteen to 136 days, but no patient had signs of nephritis. The treatment had consisted of synchronous injections of mercury and novarsenobenzol (Billon), repeated at seven day intervals.

No arsenic was found in the urine of any of these patients and all urines were free from protein and pathologic sediment. Bile pigment was found in the plasma in eleven cases, and oxidative activity in the urine was low in the severe liver cases. Hypercholesterolemia was found in nearly all the toxic cases and seemed to be an early sign of toxic jaundice. Carbohydrate metabolism was normal. Blood urea nitrogen and uric acid were generally increased.

The authors state that exercise should be carefully regulated as it tends to have a deleterious effect on debilitated patients. They are also led to believe in a rich carbohydrate diet, very low in fat and protein. This diet should be instituted before treatment is begun and continued throughout its course. Delayed poisoning by arsenic is explained by the decrease in excretory powers of the kidneys, increase of the waste products in the blood, lowered resistance of the liver to toxins and an increase in the diet proteins.

Jamieson, Detroit.

WIE IST DIE RADIKALE FRUEHHEILUNG DER SEROPOSITIVEN PRIMAR UND DER FRUEHSEKUNDAEREN SYPHILIS AM SICHERSTEN ERREICHBAR? (HOW CAN THE RADICAL CURE OF PRIMARY AND EARLY SECONDARY SYPHILIS BE BEST ATTAINED?) Habermann and Sinn, Dermat. Zeitschr. **29**:321, 1920.

The patients who have passed the negative Wassermann phase of primary syphilis are best treated by two or three courses of arsphenamin (in the practice of the authors, neosalvarsan, sodium salvarsan and silver salvarsan) and mercury. A single course, even if the Wassermann reaction becomes negative, is not sufficient and the patient is not entirely cured, as is proved by the occurrence of the relapse syndromes. The course consisted of the injection of from eight to ten doses, beginning with 0.3 gram and ascending to 0.6 gram, at intervals of from five to seven days. Gray oil was administered unless counterindicated. A period of from six to eight weeks constituted the rest interval. The second course was given even if the Wassermann reaction had been persistently negative during treatment. The authors found their patients free of symptoms clinically and serologically for a year or longer after this two course therapy. Although they have not had opportunity to study the spinal fluid, they believe from the clinical study of the patients that cerebrospinal involvement was not present. Patients with chancre, who do not give a positive Wassermann reaction at any time, may do without the second course, although the writers are reluctant to forego the "safety" course even in these patients. Mercury is thought to be an essential part of the cure of syphilis and should be used in the treatment of the disease. Arsphenamin alone may suffice in the prophylaxis of syphilis if no symptoms are manifest, as in a wife of a known syphilitic, etc.

Goodman, New York.

COCCIDIOIDAL GRANULOMA, INCLUDING THE FIRST REPORTED CASE EAST OF THE MISSISSIPPI. Kenneth M. Lynch, Southern M. J. **13**:246 (April) 1920.

Lynch reports an unusually interesting case of coccidioidal granuloma in a colored woman who, admitted to the hospital in a delirious condition which lasted until death, was thought to have tuberculosis. The illness had begun about two months before the patient was seen, when a severe attack of supposed influenza developed. The patient was in bed for three weeks, and was then up for two weeks, but was unable to do any work. She again returned to bed, where she remained until death. On her entrance to the hospital her pulse was weak and its rate 136, respiration 44 and temperature normal. The patient showed extreme emaciation; râles and areas of consolidation were found at the apex of the right lung, and a lesion described as a bedsore was present on the right buttock. Death occurred three days later.

Necropsy aroused some doubt as to the correctness of the diagnosis of tuberculosis. Gross necropsy findings were recorded as several empty cavities in the apex of the right lung, with complete but delicate encapsulation and no surrounding tubercle formation, some toughness and emphysema of the lung generally, edema of the lungs, parenchymatous degeneration of the heart and acute nephritis.

Lynch, following a hasty examination of a microscopic slide was about to pass the case as one of tuberculosis, but he noticed a peculiar body within a giant cell, and on further study was able to identify this as coccidioides immitis and to discover many of the parasites, as well as miliary lesions, in the liver, spleen, pancreas, kidneys and lungs.

While the lung lesions resembled tuberculosis rather closely, the vascularity, the lack of focal organization as tubercles, the character of the giant cells and the lack of multicellular necrosis, particularly of caseation, seemed to furnish differentiation.

The author believes that the atrium of infection was the lung, where the apparently oldest lesions were found, while other organs were involved through hematogenous spreading.

In examining the literature Lynch finds that sudden onset, much like the acute febrile diseases, has been seen in some cases of this disease, while in others the onset has been so gradual that the patient was not aware of his illness. In concluding his report, the author suggests that cases of uncertain tuberculosis in which the organism cannot be found, should be examined for this or kindred infection.

SENEAR, Chicago.

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. JOHN A. KOLMER and TOITSU MATSUNAMI, Am. J. Syphilis **4**:278 (April) 1920.

This is a report of a study of several hemolytic systems used to conduct complement-fixation tests in syphilis: (1) to determine their relative delicacy, and (2) to determine the influence of natural antisheep hemolysin in human serums. The authors conclude:

1. With the technic employed, comparative complement-fixation reactions with 503 serums from syphilitic persons under treatment have shown that tests conducted with antihuman and antichicken hemolytic systems were somewhat superior in sensitiveness to those conducted with antisheep and antiox systems.
2. From 2 to 10 per cent. more serums from syphilitic persons react positively in an antihuman system than in an antisheep system.
3. An antiox hemolytic system is more sensitive than an antisheep system yielding from 2 to 5 per cent. more positive reactions with the serums of syphilitic persons.
4. Antihuman and antichicken hemolytic systems are of about equal sensitiveness in complement-fixation tests with heated human serums.
5. The differences in delicacy of reactions conducted with antisheep, antihuman and antichicken hemolytic systems were more apparent in tests conducted with 0.01 to 0.001 c.c. of each serum than in tests conducted with 0.1 c.c. serum.
6. Natural hemolysins in human and guinea-pig serums, and particularly antisheep hemolysins, reduced the delicacy of complement-fixation tests conducted with an antisheep hemolytic system after the method described, particularly if the results were read after the tubes had stood for sixteen hours or longer in a refrigerator; antihuman and antichicken hemolytic systems were more sensitive and served to detect smaller amounts of syphilis antibody in human serums.

TOMLINSON, Omaha.

ZWEI FAELLE VON "FOX-FORDYCES KRANKHEIT (TWO CASES OF "FOX-FORDYCE DISEASE"). C. RASCH and A. KISSMEYER, Dermat. Ztschr. **29**:196 (April) 1920.

The authors give a summary of the literature with reports of all cases heretofore reported by Fox, Fordyce, Haase, Withers and others as a rare papular disease affecting the axillary region. They report two new cases of this dermatosis which may be included in the group of "neurodermite chronique circonscrite" of Brocq. One of the cases was that of a woman of 33 who had suffered from intolerable itching of the axillae, pubes and areolar of the mammae for ten years. The second patient was a woman of 24 who four years previously noted the itching papular eruption of the axillae, pubes and areolar mammae. Only regions with adult hair growth are affected, lanugo hairs being free. The papules of the disease are perifollicular, conical, brownish or reddish brown in color. In the second case many hairs had been destroyed. The area about the disease is lichenified. The itching is intense and in the younger woman required opiates.

Treatment with roentgen ray was not promising.

The microscopic picture revealed a hyperkeratosis, parakeratosis and acanthosis with infiltration of large epithelial cells in the corium. The hypertrophy of the rete malpighi was especially marked about the hair follicles and the excretory system of the sweat apparatus. In the corium there was an infiltration about the hair follicles and sweat ducts which appears to be characteristic of the affection, although Rasch notes that he has observed a similar condition in another disease attended by intense itching, namely, "prurigo nodularis."

The writers intend to use filtered rays in an effort to cause atrophy of the hair follicles and sweat ducts with the hope of curing the condition.

Goodman, New York.

PRURITUS VULVAE: ITS SIGNIFICANCE AND TREATMENT.

P. Brooke Bland, Therap. Gaz. **36**:3 (March) 1920.

Pruritus vulvae is not a specific entity but a manifestation of some local or systemic affection. The etiology of the condition may be classified under physiologic and pathologic etiology. The pathologic causes depend on local or systemic disease. The most common physiologic condition associated with pruritus is menstruation. Pregnancy, however, is the most common physiologic cause.

Systemic causes in order of frequency are: glycosuria, diabetes, nephritis, acidosis, neuroses, auto-intoxication and endocrine dysfunction. Local causes are: excessive acidity of the vaginal secretion, profuse leukorrheal discharge, purulent discharge, highly acid urine, uncleanliness and foreign body irritation. In fact all local lesions of the vulva productive of irritation are constantly associated with pruritus. Seligman claims to have isolated a diplococcus in the so-called idiopathic cases.

Four distinct skin lesions occur in pruritus: first, superficial desquamation with ulceration; second, hyperplasia or fibrosis; third, atrophy or sclerosis; and fourth, discoloration.

The milder cases, the author states, are cured by the removal of the cause and local cleanliness. In the more violent types the vulva is shaved and then scrubbed with a coarse cloth saturated with 2 drams of tincture of green soap in a quart of warm water. The scrubbing should be continued for two or three successive days. The external parts are then given a generous painting with pure tincture of iodin. The vulva is then washed vigorously with tincture of green soap every morning and evening. After washing, the parts should be dried thoroughly and a 3 per cent. solution of iodin in albolene applied. In addition, the patient is told to use an alkaline douche twice daily.

Levin, New York.

DE L'INFLUENCE DES TRAITEMENTS INSUFFISAMMENT ACTIFS SUR L'APPARITION DES SYPHILIS MENINGES (THE INFLUENCE OF INSUFFICIENTLY ACTIVE TREATMENT ON THE DEVELOPMENT OF MENINGEAL SYPHILIS).

Marcel Picard, Paris méd. **10**:211, 1920.

Picard, granting the existence of two strains of *Spirochaeta pallida,* with predilection for the skin and nervous system, respectively, thinks it possible that a dermatropic strain may be changed into a neurotropic. Not only insufficient treatment, but also active treatment may favor syphilitic attack on the nervous system, if the dosage has been too small, the series too short, or if there has been too long an interval between courses. The treatment is active enough to prevent the appearance of cutaneous accidents, and to cause the spirochetes to move toward the nervous system, where they are less vulnerable. It is because of this mechanism that we have seen so many accidents resulting in nervous diseases, ocular paralysis, etc., following the first therapeutic attempts with 606, but this therapeutic neurotropism appears possible after mercurial as well as after arsenical therapy.

He concludes: From the point of view of neurotropism, the little active agents, the benzoate, biniodid and pills are dangerous; small doses of strong therapeutic agents are dangerous; single series or long intervals between treatment with active agents are dangerous. At the beginning of syphilis, the treatment should be intensive and the therapeutic agent used in doses surely spirocheticidal. After the first treatment the rest period should be short, and treatment should be continued until clinical signs, blood serum and spinal fluid are negative.

Senear, Chicago.

PLEURALITY OF SPIROCHETES OF SYPHILIS. P. Pagniez, Presse méd. **28**:266 (May) 1920.

Pagniez believes that the researches of Levaditi and others lend plausibility to the view that the syphilitic spirochetes which produce cutaneous manifestations—the dermatropic—and those which produce paresis—the neurotropic—are different strains. In favor of this view he adduces the following facts:

Animals that have been inoculated with one strain will show a chancre when inoculated with the other strain.

The dermotropic strain after passage through rabbits continues pathogenic for monkeys; the neurotropic strain, on the other hand, after a single passage through a rabbit loses its virulence for monkeys.

A rabbit after recovery from a chancre from the dermotropic strain was inoculated in one testicle with the dermotropic strain and in the other with the neurotropic strain. The dermatropic inoculation did not develop, while the neurotropic strain developed a chancre.

In animal experiments the incubation period of the dermotropic strain was about six weeks; that of the neurotropic, four months.

The lesions produced by the two strains were of different character.

Ketron, Baltimore.

LES ACRODERMATITES SUPPURATIVES CONTINUES (CONTINUOUS SUPPURATIVE ACRODERMATITIS). E. Bodin, Paris méd. **10**:185 (March) 1920.

In this instructive and exhaustive paper Bodin discusses the subject of chronic suppurative acrodermatitis: the clinical course and appearance of the eruption, its differential diagnosis, etiology and pathologic anatomy and treatment are considered in detail.

He finds that from the ordinary pyodermatitis of the fingers it may be distinguished by the successive attacks of pustules, their arrangement in sharply defined patches without neighboring isolated lesions, the absence of lymphangitis and adenitis, and the characteristic course of the malady. The fact that the primary lesion is pustular rather than vesicular differentiates it from ordinary and ringworm eczema. The characteristic vesicles, the location on the lateral surfaces of the fingers and the evolution of the eruption seen in dyshidrosis usually prevent difficulty. Dermatitis repens offers the greatest difficulty in diagnosis, but the preceding injury and the characteristic spreading margin distinguish this disease. Bodin compares the characteristics of chronic suppurative acrodermatitis with those of dermatitis herpetiformis and finds that cases of the latter, limited to the extremities, have many points in common with the former disease.

In discussing etiology, Bodin finds evidence to show that the two common theories, i. e., origin from staphylococcus infection or from a trophoneurosis, are not tenable. He believes that chronic suppurative acrodermatitis is related to certain localized types of dermatitis herpetiformis. In support of this theory he offers the following facts: coincidence of the two diseases in two cases of Carle's, the appearance of extensive, polymorphous, erythematous pustular eruptions in cases of acrodermatitis; the beginning of the disease by a persistent and localized erythema; the itching, prickling, burning and shooting sensations; the occurrence of successive attacks and the general good health of the patient.

Bodin recalls that nearly everything has been used in the treatment of the disease, and states that he has had the best results from applications which are protective and mildly antiseptic, while radiotherapy has been of value in rebellious cases.

SENEAR, Chicago.

THE ACTION OF MERCURY OXYCYANATE ON THE WASSERMANN REACTION. IRVING SIMONS and R. L. JONES, Urol. & Cutan. Rev. **24**:6 (June) 1920.

The authors studied the action of mercury oxycyanate, administered by deep injection, on the blood serums of sixty-six syphilitics who showed strongly positive Wassermann reactions. Nearly all of them were in the late tertiary or latent stage of the disease. Some of the patients received treatment and Wassermann tests during a period of sixteen months. The average duration of treatment was 5.9 months. Good results were obtained in twenty-one cases; fair results in seventeen cases. For practical purposes one could combine these results and say that an adequate result was obtained in thirty-eight cases (57.5 per cent.). In the twenty-one cases in which good results were obtained, it required an average of 14.17 c.c. of a 1 per cent. solution of mercury injected during 2.6 months to produce a negative Wassermann reaction. These cases were then treated for two additional months, receiving totally an average of 29.94 c.c. of mercury in order to render the Wassermann reaction thoroughly negative. Comparing this with the results obtained with the arsphenamin preparations it would seem that this mercurial preparation is unusually potent. Mercury oxycyanate has few untoward effects and can be given intravenously as well as intramuscularly.

LEVIN, New York.

CONSIDERATIONS SUR LA PHYSIOLOGIE PATHOLOGIQUE ET LA PATHOGENIE DE L'URTICAIRE (OBSERVATIONS ON THE PATHOLOGIC PHYSIOLOGY AND PATHOGENICITY OF URTICARIA). A. LOUSTE, Paris méd. **10**:198, 1920.

Louste, who is led to believe that all cases of urticaria whether of external or internal origin are due to anaphylaxis, discusses the various theories advanced as to the rôle of the blood, blood vessels, nervous system, etc., in the production of the eruption.

He states that the studies which he has just reviewed allow urticaria to be considered as an expression of anaphylaxis. It seems to result from the introduction into the organism, by various routes, of heterogeneous substances of which the albuminoids are best known. Under the influence of these different substances, which have been demonstrated in the blood serum and in the urine, the cells of the organism react with marked intensity, but in a fashion relatively identical. There is a more or less intense shock of the nervous system, with hemoclasic shock, and peripheral manifestations; itching, placque formation, edema of mucous membranes, accompanied or not by various phenomena such as dyspnea, diarrhea, albuminuria, etc.

The author then reviews the three theories explaining the mechanism of anaphylaxis; the chemical theory of Richet, the biologic theory of Friedländer, and the physical theory of Besredka, Wassermann and others.

The various methods of treatment are likewise reviewed.

Senear, Chicago.

FORDYCE'S DISEASE AS PSEUDO-KOPLIK SPOTS, AND A CAUSE OF MISTAKES IN THE DIAGNOSIS OF MEASLES. Joseph C. Regan, Am. J. Dis. Child. **19**:455 (June) 1920.

Fordyce's disease is a chronic disease of the mucous membrane of the mouth and lips, which is characterized by the presence of whitish or yellowish, scanty or abundant, discrete, aggregated and often coalescent miliumlike bodies, occurring more especially on the inside of the mouth, laterally along the line of the teeth as far back as the last molar, and possibly somewhat less frequently on the vermilion or mucous and inner surface of the lips. The lesions are from pinpoint to pinhead in size, and are usually a pale buff or oatmeal color.

Fordyce spots are often mistaken for Koplik spots when they exist in patients developing German measles, and in patients ill with various contagious diseases and exposed to measles.

Well marked cases of Fordyce's disease are unusual in young children; the disease is most commonly seen in young adults and older children.

A differential diagnosis between Fordyce spots and Koplik spots is not difficult if the mouth is examined in sunlight—or at least daylight, and the color, arrangement, distribution, evolution, size and location of the lesions taken into consideration. In a few cases Koplik spots and Fordyce spots were seen together; their appearance is entirely different.

Oliver, Chicago.

THE IMPORTANCE OF INTERNAL TREATMENT IN DERMATOLOGY. THE USE OF CACODYLATE OF SODA IN LARGE DOSES AND OF SODIUM HYPOSULPHITE. P. Ravaut, Presse méd. **28**:73 (Jan. 28) 1920.

Ravaut believes that in the epidermophytic dermatoses the question of "soil" is an important one. Given a number of persons exposed in a similar way, and some will become affected with parasitic or fungous diseases of the skin, while others will escape. He does not believe that this is due to any special cutaneous sensibility, but rather to modifications of the body fluids or visceral alterations. He says that he has observed the disappearance of parasitic dermatoses after the administration of internal treatment alone. He reports over eighty-five cases of eczema in which the patient had received from 30 cg. to 1 gm., every one to three days, of a 10 per cent. solution of sodium cacodylate intravenously administered. The course of treatment lasted three weeks, and a total of from 15 to 20 gm. of the drug were used. The results were uniformly good, the drug being well tolerated. Excessive pigmentation occurred in one case of Duhring's disease. Sodium hyposulphite by mouth seemed to relieve quickly the anaphylactoid erythrodermias following the administration of arsphenamin. A solution of the drug, in 20 per cent. strength, in doses of from 4 to 15 grains daily, was injected intravenously with good results in cases of erythema, urticaria, furunculosis, eczema and dermatitis artefacta. One case of tinea versicolor disappeared without external treatment. A case of cervical trycophytosis improved rapidly.

Bechet, New York.

A METHOD FOR DEMONSTRATING SPIROCHAETA PALLIDA IN REGIONAL LYMPH GLANDS. Edwin W. Schultz, J. A. M. A. **75:** 176 (July 17) 1920.

Schultz describes a modification of the method usually employed in securing material from lymph glands for dark field examination. He claims that merely puncturing the gland and making suction with the syringe without first injecting a small amount of fluid, gives comparatively poor results. By using the method as described, he has found *Spirochaeta pallida* in practically every case of untreated syphilis. A 2 or 5 c.c. hypodermic syringe with a sharp needle is employed. Into the syringe is drawn from 0.5 to 1 c.c. of sterile physiologic sodium chlorid solution. The gland is firmly fixed between the first two fingers and thumb of the left hand, and with the syringe in the right hand the needle is passed through the overlying skin and then gently through the capsule of the gland. The point of the needle is then rotated in order to break down some of the gland tissue. After this has been done, the saline solution is slowly injected into the gland, and the capsule swelling under the finger is noted, after which the point is rotated a few times more. Suction is then made with the plunger of the syringe and as much as possible of gland-pulp mixture is withdrawn, a few drops being generally quite sufficient.

Waugh, Chicago.

CONTRIBUTION A L'ETUDE DU XANTHOME PAPULEUX GENERALISE (CONTRIBUTION TO THE STUDY OF GENERALIZED PAPULAR XANTHOMA). L. Spillman and Watrin, Paris méd. **10:** 193, 1920.

Spillman and Watrin regard xanthelasma, xanthoma tuberosum and xanthoma diabeticorum as clinical variants of a single disease. After reviewing the characteristics of the various types, they report an interesting case of generalized papular xanthoma occurring in a girl of 9 years. The patient suffered with polyuria with polydipsia, while the blood serum showed an increase in the cholesterin content. The interesting features in the case were the multiplicity of lesions, the marked diminution in the elimination of urea and the hypercholesterinemia.

After histologic study of the case, the authors feel that in their case a functional defect of the liver produced the hypercholesterinemia, and likewise an insufficient oxidation of fats, but they cannot support Chauffard and Grigant in their view that the excess cholesterin attacks the connective tissue cells of the derma.

They suggest that treatment in the widespread cases must of necessity be of a general nature, since the multiplicity of the lesions makes local treatment difficult, and they feel that a regimen directed toward the reduction of cholesterin offers the most hope.

SENEAR, Chicago.

LYMPHOCYTES AND CANCER IMMUNITY. FREDERICK PRIME, J. Cancer Res. **5**:105 (April) 1920.

The experiments were carried out with rats rendered immune to Flexner-Jobling rat carcinoma by previous inoculation, rats resistant to this tumor and rats resistant to Jensen rat sarcoma. The treated rats were given unfiltered roentgen rays from a Coolidge tube on five consecutive days for a total of 10 Holzknecht units.

Total white and differential blood counts were made before commencing the exposures, two days after the last exposure and subsequently at frequent intervals. Forty-eight hours after the completion of the last roentgen-ray exposure all the animals were inoculated with Flexner-Jobling rat carcinoma (or Jensen sarcoma). An enormous reduction in the lymphocytes, which in most cases remained low for a longer period than required for an inoculation "take," was obtained by the irradiation.

These experiments, carried out with a larger number of animals, carefully controlled, results duplicated and sources of error eliminated, proved definitely that a marked reduction in the circulating lymphocytes was not followed by any appreciable decrease in the immunity of these animals to tumor inoculation.

H. R. FOERSTER, Milwaukee.

KLINISCHER BEITRAG BETREFFEND DIE BEZIEHUNG VON HYPOTHYREOSE ZU DYSTROPHISCHEN VERAENDERUNGEN DER HAUT (RELATION OF HYPOTHYREOSIS TO DYSTROPHIC CHANGES OF THE SKIN). FRIEDERICH FISCHL, Dermat. Ztschr. **29**:201 (April) 1920.

Fischl gives a list of diseases that either through clinical evidence or through theoretical reasoning are caused by malfunction of the internal secretion of the thyroid gland. He reviews the contributions of last decade on the relation to the glands of internal secretions and the skin, with emphasis on the thyroid.

He reports a case in which inflammation of the thyroid accompanied typhoid. The skin of the entire body of the patient became grayish, distinctly thinned, cool, dry, and because of the atrophy of the subcutaneous fat, easily lifted from the underlying structures. The hair had become thin and areas of baldness were evident. The nails had become brittle and furrowed. Twelve teeth had been lost during the preceding three months. Thyroid medication was followed by marked improvement in the general condition and the skin improved in thickness, color and resilience. The nails lost their brittleness.

The case is thought to be exceptional in that the skin and adnexa alone were affected, and that edema and concomitant evidence of hypothyroidism were absent.

GOODMAN, New York.

EFFECT OF THERAPEUTIC DOSES OF MERCURY ON THE KIDNEYS AND THE DURATION OF ITS EXCRETION. L. G. Beinhauer, Am. J. Med. Sc. **159**:897 (June) 1920.

Mercury is detected by means of copper dust in an acid solution of the material tested, the copper taking up all mercury. The compound is collected, dried and heated, the vaporized mercury being deposited as an amalgam in a small particle of gold leaf.

The patients were thoroughly examined to exclude any possibility of previous mercurialization and suitable patients were given, serially, doses of calomel, ¼ grain every fifteen minutes, the total amount varying from ¼ grain to 2 grains. It was found that the excretion began from six to twelve hours after ingestion and may continue for six days if the dose is sufficiently large. The rate of excretion is the same for large and small doses, the kidneys not being injured during the process although many analyses of the urine showed temporary traces of albumin and a few hyaline casts.

Jamieson, Detroit.

RHINOPHYMA. M. G. Seelig, Surg., Gynec. & Obstet. **30**:394 (April) 1920.

Seelig describes the clinical features of rhinophyma and quotes the pathologic description from Dr. Martin Engman's forthcoming book on "Diseases of the Skin": "Rhinophyma is a familial disease representing some type of hereditary transmission. It occurs usually in the seborrheic type of individual. . . . The future rhinophyma subject shows a tendency toward flushing of the face on entering a warm room, after meals or under excitement. This flushing leads in time to chronic congestion, with secondary chronic infection of the skin of the nose and sometimes of the cheeks. This in turn leads to a chronic productive inflammation with vascular dilation, connective tissue formation and dilatation of the sebaceous glands into cyst formations. There is a marked thickening of the cutis vera, which throws the skin into folds and furrows. The end-result is the multiple formation of knobs or tumor-like masses."

The treatment is exclusively operative.

Goodman, New York.

A CASE OF EXTRA-MAMMARY PAGET'S DISEASE OCCURRING IN THE AXILLA, ASSOCIATED WITH CONDYLOMATA ACUMINATA IN THE EXTERNAL GENITALIA. Y. Satani, Brit. J. Dermat. & Syph. **32**:117, 1920.

Satani's patient was a man, aged 74, who had for six years had a patch of Paget's disease in the right axilla, which had been preceded by a wart in this location. In addition, the penis and scrotum were the site of an extensive growth of condylomata acuminata, which had developed some five years previously on some erosion of the penis. The entire patch of Paget's disease was excised and recovery was complete. The condylomata were treated successfully with roentgen rays and local applications.

The results of a histologic examination of the axillary lesion were compared with the findings in a case of mammary Paget's disease examined before and after radium treatment. As a result of this examination Satani concludes that Paget's disease may originate from any epithelial cell in loco;

local epidermis, sweat or sebaceous glands. He cites the occurrence of the disease in various parts of the body as evidence that the origin of the disease depends only to a slight extent on the specific structure of the local skin.

SENEAR, Chicago.

CALOR DE FIGO (TINEA ALBIGINA). E. VON BASSIEWITZ, Arch. Rio-Grandenses Med. **1**:55, 1920.

"Calor de figo" is the common name given to a dermatomycosis of chronic evolution often seen in the country districts of Rio Grande do Sul (Brazil). This dermatosis affects the colored races, and as a rule remains localized to the soles of the feet and the toe nails, although sometimes it involves the hands. Its principal characteristics are: hyperkeratosis with deep fissuring, achromia and keratoid onychia. The patients complain of intense pruritus and pain. The author has isolated a fungus (trichophyton?) which he has been unable to classify. The disease is similar to that observed by Jeanselme in Cochinchina under the name of Khi-Huen. Nieuwenhuis has observed in Java a dermatomycosis the clinical appearance of which is much like that of "calor de figo." He describes it under the name of tinea albigena.

PARDO-CASTELLO, Havana.

THE USE OF STOCK OR AUTOGENOUS VACCINES IN THE TREATMENT OF FURUNCULOSIS. A. MAUTÉ, Presse méd. **28**:64 (Jan. 24) 1920.

Mauté divides the vaccine treatment of furunculosis into two phases, curative and preventive. In the curative phase, he employs stock vaccine. When rapid results are desired, he injects intravenously ten million staphylococci on the first day, fifteen million on the second day, and twenty million on the third day. Two days later a second injection of twenty million is made. Immediate results are far superior with the intravenous method than with the subcutaneous. In the preventive phase, he uses an autovaccine consisting of five hundred million cocci to 1 c.c. in the following doses: first injection, 0.5 c.c.; second, three days after the first, 1 c.c.; third, four days after the second, 1.5 c.c.; fourth, five days after the third, 2 c.c.; fifth, five days after the fourth, 2 c.c.; sixth, seven days after the fifth, 2 c.c.

BECHET, New York.

THE MEDICAL AND SOCIAL CARE OF SYPHILIS AT THE WASHINGTON UNIVERSITY DISPENSARY. RICHARD S. WEISS and ADOLPH H. CONRAD, Am. J. Syphilis **4**:253 (April) 1920.

This article reveals the workings of a well-conducted clinic for the handling of syphilitic patients. Three factors were considered from the standpoint of efficiency: (1) the aspect of the problem from the public health standpoint; (2) the reaction of the patient and his family to the measures used for their own protection, health and comfort; (3) the clinical results of treatment. Of these three, the first is considered most important.

Numerous forms showing the patient's history, record of treatment, "follow-up" activities, etc., accompany the article.

TOMLINSON, Omaha.

FURTHER OBSERVATIONS ON THE PRESENCE OF ARSENIC IN THE SPINAL FLUID.

George W. Hall, Russell J. Callender and Edward S. Holmblad, Arch. Neurol. & Psychiat. **3**:631.

For these experiments the authors chose patients who had not previously received any form of intravenous medication. Eighteen patients were given the treatment. Serum from the patient's blood was injected into the spinal canal, and at intervals of from four to eleven hours after an arsenical preparation was given intravenously. At different intervals after the intravenous injection, the spinal fluid was withdrawn and tested for arsenic.

No attempt was made to estimate quantitatively the amount of arsenic present. The experiments were made in an attempt to develop a safer and more effective method than the Swift-Ellis.

The authors concluded that arsphenamin given intravenously in 0.6 gm. doses might be detected in the spinal fluid in from 25 to 35 per cent. of cases, and that irritation of the meninges by the injection of autoserum into the spinal canal does not increase this percentage.

Oliver, Chicago.

DAS ERSTE JAHR DES BESTANDS DER ANSTALT FUER KRAETZE-SCHNELLKUREN IM WILHELM INENSPITAL (EXPERIENCES SCHNELLKUREN IM WILHELMINENSPITAL (EXPERIENCES TREATMENT OF SCABIES IN WILHELM HOSPITAL, VIENNA).

Moritz Oppenheim, Wien. klin. Wchnschr. **33**:102, 1920.

The incidence of scabies having increased greatly, and ordinary methods of treatment being found too time consuming, a "rapid" treatment was begun at the Wilhelm Hospital which takes only three hours. About 12,000 patients have been treated, with few recurrences. The patient is stripped and thoroughly smeared with soft-soap for fifteen minutes. A bath at 30 C. follows, during which soft-soap is rigorously brushed into the skin, especially the points of predilection of the burrows. After the bath the patients are dried, and sulphur (Hardy's formula or one of its modifications) is employed. The patient is then wrapped in sheets and the hands and feet are gloved for two hours, after which another bath follows, and the salve is washed off with soap. Drying and anointing with zinc salve complete the cure. The clothes are sterilized by dry heat.

Goodman, New York.

FIBROMA SIMPLEX.

Louis Savatard, Brit. J. Dermat. & Syph. **32**:378, 1920.

Savatard describes a tumor appearing on the upper arm of a young girl. The lesion was small, slightly raised above the skin surface and movable with it, its surface being smooth and the color reddish brown. The tumor, which was extremely hard, had been present for three months.

Microscopically the tumor consisted almost entirely of spindle-celled fibrous tissue, with numerous smooth muscle fibers at the periphery. The growth caused a thinning and stretching of the papillary body, and the hair follicles and sebaceous glands were pressed aside.

Senear, Chicago.

SEROLOGIC RESEARCHES IN PRIMARY SYPHILIS. Clément Simon and Pierre Gastinel, Ann. de dermat. et syph. **7**:97 (March) 1919.

Simon and Gastinel made serologic studies in ninety cases of primary syphilis. The Bordet-Wassermann technic and the method of Hecht were used in conjunction. The Hecht reaction was more constant, it appeared earlier, and lasted longer than the Bordet-Wassermann reaction; on the other hand, it is exposed to errors sometimes difficult to avoid, owing to the complex nature of its technic; it should therefore not be used alone, but in conjunction with the Bordet-Wassermann technic, thereby uniting the sensibility of the former with the precision of the latter.

Bechet, New York.

WASSERMANN REACTION AND MISCARRIAGES. Herman Goodman, Surg., Gynec. & Obstet. **30**:368 (April) 1920.

Eighty-seven per cent. of 1,320 pregnant women were negative to the Wassermann test. Only 6.7 per cent. gave a + + + + reaction, and in 2 per cent. the Wassermann was + + +. Of the Wassermann negative multipara, 37 per cent. had suffered one or more miscarriages as compared to 52 per cent. of the + + + + cases. No + + + + Wassermann patient gave a history of having been pregnant more than six times. Only one woman among the 1,320 knew she was infected, although approximately one woman out of each eleven gave a strongly positive reaction.

Goodman, New York.

ANOMALOUS FORMS OF PAPULOPUSTULAR SYPHILIDS. Civatte, Ann. de dermat. et syph. **7**:123 (March) 1919.

The author reports two cases in which oval, more or less dark red, squamous, infiltrated plaques were found on the trunk and legs of the patients. On the edges of these plaques were isolated lesions covered wth a squamous scale or crust. Others were frankly pustular. The dimensions of the papules were 2 or 3 mm. On the shaft of the penis were discrete vesicopustules on a reddened, rounded base; they contained a drop of bright yellow pus, and were acneform in appearance.

Bechet, New York.

L'ECZEMA TUBERCULIDE (THE ECZEMATOID TUBERCULID). G. Milian, Paris méd. **10**:206, 1920.

The possibility of a tuberculous origin of many cases of eczema was called to Milian's attention by the case of a man who had two attacks of eczema, each coincident with an attack of pulmonary tuberculous marked by hemoptysis. Further observation has led him to believe that 80 per cent. of all cases of vesicular eczema are merely a symptom expressive of tuberculosis or, as he expresses it, "the syndrome of vesicular eczema is a tuberculide in 80 out of 100 cases." He states that every time he has searched for tuberculosis in an eczematous patient, he has found it; sometimes in an acute stage, but usually latent, sclerous, osseous, glandular, etc., in type—a general tuberculous soil.

Milian believes that a tuberculous microbic theory explains all the etiologic and clinical characteristics of vesicular eczema and its evolution, and he cites the association of the disease with tuberculids and true tuberculosis of the skin in support of his theory.

Senear, Chicago.

SEQUENCE AND ARRANGEMENT OF PALLOR AND REDNESS IN IRRITATED SKIN OF NORMAL AND DERMOGRAPHIC INDIVIDUALS. L. B. Bibb, Arch. Int. Med. **25**:680 (June) 1920.

Mechanical, chemical, thermal and electric means were employed in producing irritation on the skin of normal and dermographic persons with a striking similarity in the lesions produced as they all tended to wheal formation. The contact spot in practically all cases showed pallor immediately with a surrounding reddened zone within a few minutes.

He concludes from his experiments that the tissues studied tend to react in stereotyped manner to all the irritants investigated.

Jamieson, Detroit.

UEBER EINEN FALL VON IODODERMA TUBEROSUM (CASE OF IODERMA TUBEROSUM). Georg Tiefenbruner, Dermat. Ztschr. **29**:206 (April) 1920.

Following the taking of about twelve teaspoonful doses of potassium iodid (5 grains in a dose), a woman of 49, with a history of bladder trouble and with a chronic nephritis, presented the lesions of iodid dermatitis, which has been described as "ioderma tuberosum fungoides," "ioderma pemphigoides tuberobullosum" and "ioderma tuberosum." The face, especially the nose, the mucous surface of the hard palate and the extremities were the sites of the eruption, and one lesion was on the back, which is ordinarily free. New lesions appeared for a week after the iodid was discontinued.

The patient died. Necropsy showed, in addition to the lesions of the skin, a chronic nephritis with contraction, myocarditis, chronic bronchitis, edema of the brain and purulent otitis media (left).

Goodman, New York.

LE SYNDROME MALIN DANS LA SYPHILIS (THE MALIGNANT SYNDROME IN SYPHILIS). La Capére and Decrop, Paris méd. **10**: 203, 1920.

Struck by the great prevalence of malignant cutaneous syphilis among the native Arabs of the plains, La Capére and Decrop noticed that the natives of the mountain regions escaped these precocious lesions and were impressed with the fact that the distribution of malignant syphilis corresponded closely to the distribution of malaria. Studying along this line they found that the persons affected by malignant syphilis also had vascular hypotension. Anemia and asthenia, which apparently result from the particular malignancy of the infection, in reality account for it; they are manifestations primarily due to a pre-existing hypotension of which malaria is the principal cause among the Arabs.

Senear, Chicago.

BULLOUS ERUPTION COMPLICATING MEASLES. Frank C. Neff, Am. J. Dis. Child. **19**:469 (June) 1920.

The author reports an interesting case of an extensive bullous eruption complicating measles. The child, a girl, aged 6, developed a severe case. The temperature was 105; she had congestion of the eyes and a severe cough. Bullae began to appear in the first twenty-four hours of the measles eruption, and rapidly covered the entire body. The measles eruption was no more pronounced than one sees in well marked cases, but the lesions persisted and the color became dusky and bluish.

The bullous eruption consisted of large bullae and some vesicles, but the most pronounced feature was the far reaching separation and maceration of most of the superficial layer of the skin, which resembled an extensive burn. The child died of the measles in collapse on the fifth day.

The author concludes that he had to deal here with a distinct exanthematous disease of the nature of pemphigus, complicating or secondary to the infection of measles.

Oliver, Chicago.

ZUR FRAGE DER BLASENSYPHILIS (SYPHILIS OF THE BLADDER). C. Posner, Dermat. Ztschr. **29**:193 (April) 1920.

In an effort to learn the incidence of bladder syphilis, the author undertook the routine cystoscopic examination of all his female syphilitic patients. Among the 135 reported in this paper, he notes that not one presented undoubted evidence of syphilis of this organ, although many of the women had bladder pathology due to an antecedent gonorrheal infection. He will report later his observations on the bladder of nonsyphilitic women in order to furnish material for comparison.

Goodman, New York.

A CASE OF BLUE CHROMIDROSIS. Mario Totta, Arch. Rio-Grandenses Med. **1**:47, 1920.

The patient was a physician, aged 46, who had a neurotic temperament and had had several attacks of manic-depressive insanity. The abnormal perspiration was confined to the skin of the scrotum and the adjacent parts of the thighs, which appeared covered with blue moisture of a deep hue. There was no hyperidrosis. The chromidrosis was more marked when the patient was nervous or excited. The chemical analysis of the coloring matter found in this case proved it to be a ferric salt.

Pardo-Castello, Havana.

THE TREATMENT OF SCABIES WITH AN ALCOHOLIC SOLUTION OF BETANAPHTHOL. Sloboziaño, Gaz. d. hôp., Feb. 3, 1920, p. 181.

Sloboziano employs the following formula: betanaphthol, 28 to 40 gm.; alcohol, 90 per cent., 400 gm. This suffices for one treatment. It is applied on the dry skin without rubbing or preceding baths. The entire surface of the body is moistened. On the scrotum the solution should be diluted. The applications are made twice a day for three or four days. The solution is well borne. The author did not observe any secondary dermatitis.

Bechet, New York.

THE DIAGNOSTIC VALUE OF LYMPHOCYTOSIS IN SYPHILIS. S. Mazza and R. Corvalan, Prensa Med. Argentina **4**:35, 341.

The authors made blood examinations in 250 cases of syphilis in its different stages. In all of them the cell count showed a slight lymphocytosis of 29.16 per cent. as an average, with extreme cases of 52 per cent. and 16.33

per cent. The authors have also verified that in many normal cases and in other diseases like chickenpox, smallpox, leprosy and malaria, a similar percentage in the lymphocyte count may be observed. They conclude that true lymphocytosis begins at or above 40 per cent., that the increase in lymphocytes observed in some cases of syphilis, is not constant and high enough to be considered of diagnostic value and that the percentage should never be based on a count of less than 300.

V. Pardo-Castello, Havana.

LA DERMATOLOGIE ET LA SYPHILIS EN 1920 (DERMATOLOGY AND SYPHILIS IN 1920). Dr. Milian, Paris méd. **10**:181 (March) 1920.

In a general review, Milian discusses, as among the most important contributions to the subject of syphilis, Levaditi and Moore's study of the treponema in general paralysis, Nicolau's work on the spinal fluid in the primary stage of syphilis, Simon and Gastenel's discussion of the evolution of the serologic reaction in the course of the chancre and various studies in the treatment of syphilis, the icterus following arsphenamin treatment and the so-called arsenical erythemas. In the dermatologic field are discussed Jeanselme's work in pediculosis, Darier's discussion of the parasitic nature of dyshidrosis, and Gougerot's attempt to classify the various forms of cutaneous infections.

Senear, Chicago.

THE CALCIUM CONTENT OF THE BLOOD WITH SPECIAL REFERENCE TO CANCER. Otto Krehbiel, J. Cancer Res. **5**:199 (April) 1920.

In cancer the average blood plasma calcium content was found to be within normal limits and no characteristic concentration accompanied any given type or location of neoplasm. The results were similar for benign tumors and for thromboangitis obliterans and low for severe nephritis, eclampsia and tetany. Thirty-four cases of malignant disease were studied, the calcium content varying from 5.8 to 15 mg. per 100 c.c., the average being 9.4 mg. Accepted normal figures are 9 to 11 mg.

H. R. Foerster, Milwaukee.

EIN FALL VON URTICARIA PERSTANS VERRUCOSA (CASE OF URTICARIA PERSTANS VERRUCOSA). Hans Hirsch and Walter Bruck, Dermat. Ztschr. **29**:216 (April) 1920.

Under this title, Hirsh and Bruck describe a case of prurigo nodularis in a woman of 40 years, who for four years had presented an increasing number of pruritic nodules over the body. A photograph is given. The literature is reviewed with a bibliography.

Goodman, New York.

SUBLEUKEMIC ERYTHRODERMIA WITH PSEUDO CURE. A Caesar and J. Tapie, Ann. de dermat. et syph. **7**:114 (March) 1919.

This is a report of a case of lymphadenosis and erythrodermia with spontaneous remission of the symptoms, of several months' duration, previous to a fatal termination.

Bechet, New York.

UEBER DIE VANADIUM THERAPIE BEI SYPHILIS (VANADIUM THERAPY OF SYPHILIS). Ferdinand Winkler, Dermat. Wchnschr. **70**:147 (March) 1920.

This article gives a review of the literature; nothing new.

Zimmermann, Baltimore.

NOCHMALS EIN FALL VON SOGENANNTER DERMATITIS DYSMENORRHOICA SYMMETRICA BEIM MANNE (ANOTHER CASE OF SO-CALLED DERMATITIS DYSMENORRHOICA SYMMETRICA IN MAN). A. Brauer, Dermat. Ztschr. **29**:211 (April) 1920.

This is part of a discussion concerning the identity of the so-called new dermatitis of Matzenauer and Polland.

UEBER DIE BERUECKSICHTIGUNG DER HAUT UND GESCHLECTSKRANHEITEN BEIM ZWANGSFAMULIEREN (CONSIDERATION OF SKIN AND VENEREAL DISEASES UNDER THE SYSTEM OF COMPULSORY CLINICAL CLERKSHIP). Erich Hoffmann, Dermat. Ztschr. **29**:214 (April) 1920.

This is a plea for a compulsory period of clinical instruction in skin and venereal diseases in the new curriculum. The proposal is made to include instruction in the social hygiene program (campaign against prostitution, sexual instruction), history taking and reporting.

Goodman, New York.

CONCERNING THE WASSERMANN REACTION AS THE THERAPEUTIC INDEX FOR SYPHILIS. Bernard Oettinger, Am. J. Syphilis **4**:297 (April) 1920.

In support of his view that the Wassermann reaction is not a reliable guide for treatment, the author points out those cases of late syphilis, particularly of the nervous system, which continuously react positively to the Wassermann after long continued intensive treatment and which may be done irreparable damage by such treatment. On the other hand, false security may be felt as a result of negative laboratory findings in definite syphilitic conditions.

Tomlinson, Omaha.

UEBER POROKERATOSIS (POROKERATOSIS MIBELLI). W. Bruck and H. Hirsch, Dermat. Ztschr. **29**:223 (April) 1920.

A severe case of porokeratosis in a boy of 16 months is described. There is an exceptionally good review of the literature, histology, etiology and treatment of this dermatosis. They conclude that porokeratosis belongs to the nevus group of diseases. The bibliography is complete.

Goodman, New York.

A CASE OF MALIGNANT PUSTULE, IN WHICH THE INCUBATION PERIOD WAS KNOWN. H. J. McCurrich, Brit. M. J. **1**:828 (June 19) 1920.

The interesting features of this case were: The disease started from a razor cut. The patient knew the incubation period of the papule and vesicle.

The patient, a schoolmaster, aged 36, cut himself with a razor while shaving. He was using a new shaving brush for the first time. Thirty hours later he noticed a painful pimple at the site of the cut, and twelve hours later the papule had become a vesicle. The vesicle discharged, and two days later his neck became stiff and swollen. Three days later he consulted a physician, who excised the lesion and began the administration of antianthrax serum. The patient made an uneventful and rapid recovery.

Cultures from the pustule showed staphylococci and a few anthrax bacilli; a culture of the shaving brush showed *B. anthrax,* though a guinea-pig inoculated was apparently unaffected.

If the micro-organism on the shaving brush was anthrax, its virulence apparently was attenuated.

Oliver, Chicago.

MANUFACTURE OF THE COOLIDGE ROENTGEN-RAY TUBE. R. C. Robinson and C. N. Moore, Am. J. Roentgenol. **7**:224 (May) 1920.

A brief record of the manufacture of the two types of Coolidge tubes, with photographs of some of the machinery of the laboratory and factory of the General Electric Company.

Goodman, New York.

THE ROENTGEN-RAY TREATMENT OF ACNE VULGARIS. H. C. Semon, Brit. M. J. **1**:700 (May 22) 1920.

In a well written article, the author concludes that while acne vulgaris in its early stages can be relieved in many ways by vaccines and the application of lotions and ointments containing sulphur, resorcin or mercury, a cure can only be attained by the judicious application of the roentgen rays.

The nodular and keloidal varieties of the disease are not amenable to relief or cure by any other method.

Relapses after apparent cure by roentgen rays are rare.

There are no permanent contra-indications to the treatment by roentgen rays; temporary cosmetic stigmas are sometimes encountered, but permanent disfigurement is the result of faulty technic.

Oliver, Chicago.

LIPOMAS SUBCUTANEOS MULTIPLES (MULTIPLE SUBCUTANEOUS LIPOMAS). Vicente Gimeno, Los Progr. de la Clin. **8**:268 (April 30) 1920.

Gimeno discusses the various types of subcutaneous lipomas that are ordinarily encountered, and gives a photographic clinical and microscopic study of an extensive case under his observation. His treatment was surgical, with the addition of the ingestion of thyroid extract, as good results have attended endocrine medication.

Goodman, New York.

SYPHILIS INSONTIUM. J. C. McWalter, Brit. M. J. **1**:827 (June 19) 1920.

It is generally taught that syphilis is transmitted to the fetus only at conception or in the earlier months of pregnancy. The case reported is one in which it appears conclusively that infection can take place in the eighth month of pregnancy.

The patient, a married woman in the early thirties, the mother of four healthy children, gave no history of abortion. She developed an ulcer at the angle of the mouth in which the *Spirochaeta pallida* was found—an evident chancre—and was immediately put on antisyphilitic treatment of mercury and iodids. The sore rapidly healed and in four weeks she was delivered of a healthy appearing infant. Five weeks later, the child developed unmistakable signs of congenital syphilis, which cleared up rapidly under syphilitic therapy.

Oliver, Chicago.

RECURRENT IRITIS ASSOCIATED WITH DERMATITIS EXFOLIATIVA: REPORT OF A CASE. Sanford Gifford, Am. J. Ophth. **3**:433 (June) 1920.

CATARACT PROBABLY DUE TO ROENTGEN-RAY EXPOSURE. Oscar Wilkinson, Am. J. Ophth. **3**:435 (June) 1920.

The case reported is one of double simultaneous cataract in a woman 40 years of age, with negative history and findings, with the exception of a lupus erythematosus of the face. During a two and one-half year period this patient received more than sixty unfiltered roentgen-ray exposures to the face, during which the patient's eyes were uncovered and open. A simple cataract operation resulted successfully.

Foerster, Milwaukee.

LEUKODERMIA. W. Knowsley Sibley, Proc. Roy. Soc. Med. **13**:71 (May) 1920.

An extensive case is reported.

Guy, Pittsburgh.

CUTANEOUS SARCOID OF BOECK. A. M. H. Gray, Proc. Roy. Soc. Med. **13**:63 (May) 1920.

A generalized eruption of lesions began as pinhead papules and attained the size of a sixpence piece; the well developed lesions were copper colored and of waxy appearance. Some showed definite hemorrhage on legs. When confluent, the patches became clear at the center and spread, leaving pigmented areas. Superficial ulceration was noted and considered to be of traumatic origin. There were from walnut to orange sized tumors on the bursae of elbows and knees. The lymphatic glands in the axillae and groin were enlarged. Section showed a granulomatous structure, with giant cells deep in the section; no organisms were found. There was definite improvement under novarsenobillon.

Guy, Pittsburgh.

CIRCINATE ERYTHEMA. E. G. Graham Little, Proc. Roy. Soc. Med. **13**:59 (May) 1920.

A more or less generalized eruption of erythematous lesions with distinctly raised edges (varying in size from a dime to palm of the hand), which enlarged by peripheral extension, was accompanied by factitious urticaria. The eruption had been for six months unaffected by teeth extraction and various local applications, but cleared markedly in four days under 20 grain doses of calcium lactate, three times a day.

Guy, Pittsburgh.

MORPHEA OF ACUTE ONSET. E. G. Graham Little, Proc. Roy. Soc. Med. **13**:59 (May) 1920.

A girl, aged 12, developed typical sclerodermatous patches in two weeks' time.

Guy, Pittsburgh.

ZUR NEOSALVARSANTHERAPIE BEI LUETISCHEN ERKRANKUNGEN DES HERZENS UND DER AORTA (NEOSALVARSAN IN THE TREATMENT OF SYPHILIS OF THE HEART AND AORTA). Kuno Kothny and Albert Müller-Denham, Wien. klin. Wchnschr. **33**:77, 1920.

The authors report seven years' experience in treating syphilis of the heart and aorta with neosalvarsan. They are guided by the general condition of the patient in initiating the treatment and begin with the smallest doses (from 0.05 to 0.075 gram) at intervals of three or four days. The 0.3 gram dose is considered too large even as the maximum, and the authors have restricted themselves to 0.15 or 0.2 for largest doses. Mercury is utilized in the treatment. With a more intensive administration of the drug, Romberg reported that his patients lived an average of three and a half years after treatment was begun. With the smaller doses given by the authors, the average is between five and six years if treatment is continued.

Goodman, New York.

TRADE ECZEMA. W. J. O'Donovan, Proc. Roy. Soc. Med. **13**:75 (May) 1920.

One man had a dermatitis of the hands, arms and face produced by red oil, a dyestuff. The condition was treated with acetone, which is a dye solvent, and the eruption cleared in four days. The second patient used bismarck brown in the course of leather work. The eruption was a dermatitis of the hands, arms and face.

Guy, Pittsburgh.

DIE ANSTALT FUER KRAETZESCHNELLKUREN IM WILHELMINENSPITAL IN WIEN (INSTITUTION FOR RAPID TREATMENT OF SCABIES AT WILHELM HOSPITAL, VIENNA). Franz Schönbauer, Wien. klin. Wchnschr. **33**:105, 1920.

The equipment and the administrative organization of the hospital for intensive treatment of scabies is described. The advantages in bed space and in money are given, and it is stated that only by the institution of the three-hour cure can the pandemic of scabies be conquered.

Goodman, New York.

ANESTHETIC LEPROSY. E. G. Graham Little, Proc. Roy. Soc. Med. **13**:59 (May) 1920.

A Hindu medical man, shown before the section in 1915, had an eruption on the right leg which was diagnosed as probable lichen planus or tuberculosis. Recently a very complete anesthesia of the affected areas developed, but as yet Hansen's organism has not been found either in the tissue sections or in the nasal discharge.

Guy, Pittsburgh.

LUETISCHE TRACHEOOSOPHAGUSFISTELN (SYPHILITIC TRACHEO-ESOPHAGEAL FISTULAS). Max Krassnigg, Wien klin. Wchnschr. **33**:130, 1920.

Fistula formation between the esophagus and the trachea is not rare, but syphilis is seldom mentioned as the cause of such fistulas. Krassnigg had the opportunity of studying a case from the stage of stricture to death, which was caused by an aspiration pneumonia despite antisyphilitic treatment. In cases reported in the literature, nutrition was maintained by gastrotomy and artificial feeding. Specific therapy of an existing fistula may increase it very quickly. Pneumonia usually ensues, however, and the patient dies.

Goodman, New York.

GENERALIZED RODENT ULCER. A. M. H. Gray, Proc. Roy. Soc. Med. **13**:68 (May) 1920.

A man, aged 51, with a family history of psoriasis, had epitheliomas scattered over the entire body.

Guy, Pittsburgh.

THE INTERNAL TREATMENT OF PSORIASIS. R. Saboraud, Presse méd. **28**:53 (Jan. 21) 1920.

Sabouraud reviews the various well-known dietetic and medicinal measures used in psoriasis. He has used the vaccine made by Danysz, from the microbic flora in the fecal matter of the subject, with occasional good results; but he states that as yet nothing has been found that has proved a specific in this usually rebellious affection.

Bechet, New York.

EXTENSIVE VASCULAR NEVUS. A. M. H. Gray, Proc. Roy. Soc. Med. **13**:71 (May) 1920.

A port wine mark involved the entire body except the right front side of the chest.

Guy, Pittsburgh.

SYPHILIS AND PREGNANCY. William Jackson Young, Surg., Gynec. & Obstet. **30**:508 (May) 1920.

Two hundred of 267 Wassermann examinations of pregnant women at the Louisville Public Hospital gave negative results. Fifty tests were either + + + or + + + +, and seventeen were + or + +. Few of the women presented any cutaneous evidence of the disease.

Goodman, New York.

TAR CARCINOMA. J. H. Sequeira, Proc. Roy. Soc. Med. **13**:73 (May) 1920.

Two cases of squamous cell carcinoma developing in men handling pitch are reported.

Guy, Pittsburgh.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, May 7, 1920

WILLIAM A. QUINN, M.D., *Presiding*

URTICARIA PIGMENTOSA. Presented by DRS. ORMSBY and MITCHELL.

In this patient, a woman, aged 34 years, the disorder had been present for five years, during which time the lesions had remained stationary. A biopsy had been performed but the mast cells usually found in urticaria pigmentosa were not present. The case was one of the acquired type. (For further description see the *Journal of Cutaneous Diseases* **36**:469, 1918.)

DISCUSSION

DR. NORMAN WALKER (by invitation) said he had not seen any cases of acquired urticaria pigmentosa. The cases he had seen had all been in children, but he saw very little difference between these adult cases and those in the children. Much stress was laid on the urticaria, whereas the pigmented lesion was the one of importance to the patient.

A CASE FOR DIAGNOSIS. Presented by DR. WAUGH.

An infant, aged 2 weeks, was of normal appearance at birth, but twenty-four hours afterward the skin became hard and contracted, both eyelids were markedly everted, the mouth was open, the child could not nurse and had a pale, yellowish, waxy appearance. Three or four days later numerous fine, whitish lines, not unlike scar tissue, developed. At no time was there any bullous eruption. The skin was not mottled. After about a week desquamation began and had continued to the present time. The mother had one other child, aged 4 years, living and well. There were two miscarriages between the birth of the latter child and of the patient. On the right foot was a small band of skin which retained about the same appearance that the entire body presented two days after birth; a similar condition persisted on most of the scalp. At the time of presentation the child could nurse in a normal way, looked well and was gaining. There were no palmar lesions and no eruption on the plantar surfaces, but the entire body and scalp were involved in the process.

DISCUSSION

DR. WILE did not feel that he could offer any diagnosis. He thought it a very extraordinary condition occurring at birth with an apparent sclerodactylia. Such changes might be due to syphilis. There was a history of two miscarriages; the child had the appearance of a cachectic new-born infant, such as was seen in syphilis, and the associated exfoliative dermatitis was suggestive of syphilis in the new-born. He had not seen a case with such marked sclerosis of the fingers and toes and his second thought was that the case belonged to the scleremias, a case of which was presented before the society a year or two ago by Dr. Lieberthal.

Dr. Ormsby said the part of the skin that was left on the baby, that which had not exfoliated, looked like collodion, and when the child was born it probably looked as if it were covered all over with collodion. It has been thought that that type of case belonged to the ichthyotic group, but it was proved by Bowen some years ago that that layer was the epitrichium which had not been cast off. The condition was supposed to be congenital ichthyosis, but it was not. He had seen only one other case just like this; in that case exfoliation began soon after birth but, unfortunately, the infant died of pneumonia at 3 weeks of age. He believed the case of this infant belonged in that group.

Dr. Lieberthal said that his case healed in about three months and the child was still living.

Dr. Norman Walker said he was glad to hear Dr. Ormsby depart from the theory of congenital ichthyosis, because he claimed that this should be done.

Dr. Waugh said the attending physician told him that the baby had a normal appearance as far as physical development was concerned, but it appeared exceedingly oily, and two days after birth the skin looked as though it had been painted with collodion. It seemed to him rather improbable that the child could be syphilitic. It was normal at birth but during the first week it could not nurse and the undernourished appearance was due to this. The mother's blood gave a negative Wassermann reaction.

Dr. Wile thought that the exfoliation was really of secondary interest, the most interesting thing being the sclerosis of the extremities which he had seen simulated only in the sclerodermas. Furthermore, one could not disregard the syphilitic element because the child was normal at birth, because a baby might be normal at birth and develop syphilis a few weeks afterward.

Dr. McEwen thought that since the child was improving constantly and the skin beneath the exfoliating material was practically normal the diagnosis of Dr. Ormsby was correct.

BROMODERMA. Presented by Dr. Senear.

A child, aged 14 months, had pneumonia in April and was given cough medicine for two weeks. Five days after stopping this medicine the eruption began. The lesions were still forming, some fresh ones being present on the forehead.

DISCUSSION

Dr. Foerster considered this a typical instance of bromoderma. An eruption of this degree of development and distribution is not infrequent in children who have had whooping cough and have been given patent medicines containing bromids.

Dr. McEwen concurred in the diagnosis of bromoderma.

Dr. Norman Walker agreed with the diagnosis and thought it remarkable that all over the world bromids produce these eruptions in children, not only in the form of local lesions but also largely with respect to distribution. He was not accustomed to seeing such plump children for in the towns in the middle of England during the war the women went to work shortly after the baby was born and left the children in the care of some woman who might give them teething powders to keep them quiet. The mothers knew nothing of this and the doctor was informed that the baby had been given no medicine. Why was it that potassium bromid given to children everywhere affected the same areas of the body? Dr. Walker thought this fact should be kept in mind when considering the distribution of lesions. Casts of bromoderma which he had shown in demonstrating the effects of medicines the composition of which was not known had more to do with convincing the committee of the importance of his work than had anything else.

Dr. Senear had been unable to ascertain how much medicine the child was given, but it was administered for a cough following pneumonia. He was interested to know what the cosmetic effect might be. In a similar case reported in New York after the eruption was stopped, judging from the description, the end-result was very bad, for practically every lesion left a bad scar. His experience with bromoderma was limited and he was interested to know what the outcome would be.

Dr. Ormsby stated that the cases he had seen in infants and children had cleared up without any scar formation. When bromoderma occurred on the leg below the knee in adults it left quite pronounced scarring, not unlike that seen in blastomycosis.

Dr. Norman Walker agreed that bromoderma in a child would disappear without scarring. Chronic bromoderma on the leg below the knee, especially in epileptic patients, left a scar so closely resembling syphilis that experts were often confused. He cited the case of a man who had taken enormous doses of bromid whom he was intending to present in his clinic, and a professor said it was a clear case of syphilis.

SYRINGOCYSTOMA. Presented by Dr. Lieberthal.

In a woman, aged 25, married, the mother of one healthy child, with no miscarriage, about nineteen years ago, after an attack of scarlet fever, pimples started to develop on the chest, and to a slighter degree on the abdomen, back and neck. These lesions had shown no changes whatever at any time and had caused no subjective symptoms. There was no increased perspiration in the affected places. The rest of the cutaneous surface was free. She received high-frequency treatment about seven years ago, without any beneficial results. The present affection consisted of yellowish and yellowish red nodules varying in size from that of a pin point to a split pea, mostly hemispherical, and with rounded or irregular borders. They were more numerous, larger, closely arranged and of red color on the upper part of the chest, while on the lower part of the chest, on the abdomen and back they were smaller and rather pale.

DISCUSSION

Dr. Irvine did not care to venture a diagnosis but had thought of a syringocystoma as one of the possibilities.

Dr. Zeisler agreed with the diagnosis of syringocystoma and considered it a parallel case with the one shown by Dr. Ormsby some years ago.

Dr. Senear agreed with the diagnosis but said that in one case seen recently with Dr. Pusey they were thrown off the track on account of the extent of the eruption. It occurred in sweeping lines, like a Christmas tree, and made almost a solid sheet, the lesions being very small. Some of the lesions were grouped in such a way as to present the appearance of a single lesion. The striking thing was that while for the most part the eruption was on the right side, the left side of the abdomen was involved, and a round area, with the umbilicus as its center, was entirely free. He had no explanation to offer for this.

Dr. Waugh was much interested because he had only seen one case previously that resembled this. The case shown by Dr. Ormsby several years ago had more extensive lesions, involving the arms, abdomen and thighs.

Dr. Lieberthal stated that he based the diagnosis of syringocystoma on the first appearance of the lesions in early childhood and continuation of these lesions without any change whatsoever. The result of a bioscopic examination would be reported later.

CASE FOR DIAGNOSIS. Presented by Drs. Ormsby and Mitchell.

A woman, aged 46, presented lesions which had first appeared on the face two years previously, and a year later on the posterior surfaces of the shoulders. None had disappeared. On the nose and on the cheeks were several dark red infiltrated plaques and nodules varying in size from a fingernail to a small coin, elevated from 1 to 2 mm. Over the shoulder posteriorly there was a palm-sized area of grouped and coalescing flat, pink papules and nodules, ranging in size from a match head to a small fingernail. A few smaller lesions were present on the upper arm. There were no subjective symptoms and the Wassermann reaction was negative.

DISCUSSION

Dr. Zeisler thought the lesions on the cheeks were suggestive of lupus erythematosus but those on the back did not fit in with this diagnosis.

Dr. Eisenstaedt said that his first impression was that the case resembled lupus erythematosus more closely than anything else, but he was not willing to give this as a definite diagnosis.

Dr. Wile thought the picture was confusing because of the attempt to make a single condition out of two different things. He thought the lesions on the face were erythematous lupus and those on the back simple lichenification.

Dr. Foerster agreed with Dr. Wile that the lesions on the face and on the trunk differed in character. He could not say what the lesions on the trunk were, but the lesions on the face suggested the condition of angiolupoid, as described by Pautrier and Brocq, which is probably related to the nodular types of sarcoid of Boeck. These authors describe the occurrence of small, discoid, bluish red or yellowish plaques, few in number, limited to the sides of the nose and adjacent portions of the cheek, and seen at times at the angle of the jaw. The lesions are slightly elevated, firm and smooth, and have as a characteristic feature small dilated vessels running over the surface. He would be interested to know the outcome in Dr. Ormsby's patient.

Dr. Lieberthal said that the patient had appeared in his office two weeks before and the diagnosis entered on her record was that offered by Dr. Wile. After examining the back he wanted to excise a piece for examination, and the patient said "next time," and he saw her no more.

Dr. Ormsby said that the patient came into the office two days before presentation and he presented her for diagnosis. He had the same impression that the others had of the case. Some of the lesions had the appearance of lupus erythematosus but some were too nodular. Some of the old nodular cases of lupus erythematosus had turned out to be sarcoid and this one might prove to be that disorder. He had demonstrated a case some years ago as lupus erythematosus which developed lesions of sarcoid. The lesions on the back were not sarcoid, but those on the face might prove to be that disorder.

ERYTHEMA MULTIFORME. Presented by Dr. Zeisler.

In a man, aged 20, first seen about one week before presentation, there was a history of an eruption in the mouth with rise in temperature and sore throat. Three or four days later erythematous patches appeared on the palms and backs of the hands, then on the lower extremities. They had cleared up considerably, but in the beginning they were typical of the erythema iris type of lesion. Conjunctival lesions were also present. The mouth and lips showed extensively eroded areas covered with a yellowish pseudomembrane which was very painful. Cultures and smears from the mouth lesions and the Wassermann reaction were negative. Salicylates had been administered.

DISCUSSION

Dr. Potthoff said this was a case of erythema multiforme with some of the lesions on the hands of iris type.

Drs. Stillians, Senear and Mackey agreed with this diagnosis.

Dr. Norman Walker said he thought that some of the friends with whom he had been associated in the past carried distribution to extreme lengths. In his opinion Sabouraud carried it a little too far and Dr. Smith taught his students almost exclusively on location, having devoted a large part of his life to the study and teaching of the external distribution of cutaneous lesions, though he devoted some time to the study of internal causes. Dr. Walker thought it was extraordinary that the iris lesions should always affect the hands and less often the feet, and why they selected the mouth. It was very remarkable that one should give a vaccine internally and have it produce a certain distribution. Here was a vaccine which selected certain definite areas. He considered "erythema iris" a very regrettable name; the lesions were not like a rainbow at all, but much more like a target. If one wished to depress a patient this could be done by telling him he was sure to have several other attacks. Dr. Walker thought the older books did not dwell enough on the distribution of the lesions of this disease in the mouth. He had seen cases a number of times which had been diagnosed as syphilis because of this involvement. The distribution interested him particularly. He saw many cases and was interested to know if anyone had any suggestion to offer as to whether there was a possible cause for these cases.

Dr. Lieberthal stated that in erythema multiforme the mouth was affected only in a small percentage of cases. The disease has, unquestionably, various causes. Sore throat may produce it and so may gastro-intestinal affections, while in some instances disturbances of these parts may be manifestations of the disease.

Dr. Zeisler stated that the diagnosis of syphilis had been made on this patient at Wesley Hospital, and mercury and iodids were started. He had recently had two cases of erythema multiforme at the Cook County Hospital with mucous membrane lesions. One cleared up very rapidly when a peritonsillar abscess was drained. Dr. Zeisler was under the impression that many of these cases originated from infection of the tonsils, possibly a streptococcus.

LICHEN PLANUS. Presented by Dr. Quinn.

A fireman, aged 24, presented an eruption over the arms and body that had been present for three months. The eruption started on the wrists and gradually became generalized. Some scaling was present and at times severe itching was complained of. Occasionally vesicles were present, some of them hemorrhagic. While in military service he was recognized as a typhoid carrier and in July, 1919, while in service on the Mexican border, he was badly frightened.

DISCUSSION

Dr. Michelson thought the case was one of lichen planus, and considered it interesting because of the arrangement of the lesions in rings.

Dr. Potthoff agreed in the diagnosis of lichen planus and called attention to the fact that there was some pitting or scarring, probably due to some previous trouble on the skin.

Dr. Stillians said he had hoped to present this patient at the previous meeting, but because of the fact that after the administration of ¾ grain of mercury salicylate the man developed a high temperature and broke out in vesicular eruption he did not return. The eruption was not very profuse but was widespread. He wished an opinion as to whether or not this could have been due to the salicylate.

Dr. Quinn stated that the patient was severely shocked in July, 1919, but believed this was too long ago to account for the development of these lesions. He had observed the man for four weeks and the eruption had cleared up to a considerable extent.

Dr. Irvine said that he had under observation a case of lichen planus just as generalized as this but without the circinate lesions. This man was in the hospital for a number of weeks with shell shock but the lichen planus did not develop until a number of months after that.

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

A man, aged 56, was infected with syphilis twenty years ago. Seven or eight years ago the present lesions appeared on the arms, and one year ago on the face. The lesions consisted of nodules in the skin and beneath the skin of the extensor surfaces of both forearms. Some of them were bluish red, others were the color of the normal skin. In certain areas were groups of nodules which tended to become circinate. On the left cheek was a plaque about 1.5 cm. in diameter, glossy and waxy in appearance and moderately indurated. The Wassermann reaction was strongly positive and the patient exhibited dyspnea and severe anginal pain on exertion.

DISCUSSION

Dr. Senear said the positive Wassermann reaction suggested syphilis and that was probably the proper diagnosis in spite of the lack of symmetry of late syphilis. At a distance there was a distinct tendency to a rather arciform distribution. He had also thought of the nodular tuberculous lesions of the hypoderm described by Wende, as well as of subcutaneous sarcoid.

Dr. Stillians stated that he had hastened to present the man before the lesions cleared up, and had seen him for the first time that afternoon. He agreed with Dr. Senear that the case was probably an unusual one of nodular syphilis. There were some subcutaneous plaques without any change in color of the skin over them, and he thought of the possibility of an atypical subcutaneous sarcoid, such as was shown about a year ago.

ULCER OF THE GROIN. Presented by Drs. Ormsby and Mitchell.

A man, aged 24, presented a large ulcerating lesion situated in the groin, which closely resembled the old serpiginous chancroid. The lesion followed an injury; operative procedure had been employed without result. The ulcer was soft, presented well defined edges, and a slightly suppurating floor. The bridges and undermined areas usually seen in serpiginous chancroid were absent, but the edges presented a circinate outline. Cultures produced only ordinary pyogenic organisms. The histologic section was not characteristic, merely showing the picture of granuloma.

DISCUSSION

Dr. Wile thought the case probably belonged to the group which was discussed at the January meeting, when Dr. Grindon so ably presented the record of a number of cases of ulceration in the groin which he concluded belonged to three different types: (1) the neglected chancroidal ulcer, with or without the finding of the bacillus, in which there was a direct history of exposure and a chronic ulceration of the groin; (2) the group of ulcers frequently seen in the semitropics, a report of which was recently published in the Archives of Dermatology and Syphilology, the chronic ulcerations in the pudenda, the specific organism of which had been found by Dr. Goodman in Havana, and (3) the group in which it was possible to rule out the tropical bacillus and also that of Ducrey, in which there was a chronic ulcer of the groin, the chronic, low-grade ulceration resembling closely tuberculosis, at least in the clinical picture. Dr. Wile believed this was a case of the last type, and thought that significant in this case was the extent of the ulceration on the abdomen, away from the normal lymphatics. The few cases he had seen had yielded everything bacteriologically one wished to look for—staphylococcus, streptococcus—everything but the spirochete of syphilis. All of the cases were characterized by extreme chronicity and resistant to treatment. In this case Dr. Wile ventured the diagnosis of ulceration of the groin, phagedenic in type, of unknown etiology.

Dr. Norman Walker recalled seeing a similar case thirty years ago with Dr. Barber, who published the case under the title lupus serpiginosus. The case was extremely obstinate to cure and presented the same appearance as this one.

Dr. Ormsby said the only cases he had seen like this were observed at least twenty years ago, and at that time he saw what was called "serpiginous chancroid." Those cases had a lesion on the penis, then a bubo formed and from this ulcerating bubo the lesions developed. The case under discussion was similar except that in those cases there were bridges of tissue, which were not present in this instance. This patient had no chancroid preceding the ulcer and there was no venereal history. The section shown under the microscope was not characteristic, but revealed inflammatory reaction.

DERMATITIS HERPETIFORMIS. Presented by Dr. Oliver.

A man, aged 68, presented a disorder which had been present for nine months. The lesions began as vesicles, some remaining as such and others becoming bullous. There was considerable itching. The patient also had a large umbilical hernia. There was an eosinophilia of 8 per cent., and a white blood cell count of 8,200.

DISCUSSION

Dr. Mackey thought it was a case of dermatitis herpetiformis.

Dr. Irvine considered it dermatitis herpetiformis and he was interested to see the pustular lesion, as he had rarely encountered this type in the few cases he had seen. In most the urticarial base and the subsequent pigmentation were characteristic.

Dr. Michelson was impressed with the absence of any itching or burning or any scratch marks.

Dr. Wile wondered whether a diagnosis of pemphigus could not be sustained. He felt if we were to base a differential diagnosis of dermatitis herpetiformis on grouping alone a certain number of cases of pemphigus would go as dermatitis herpetiformis. He believed it was a case of true pemphigus.

Dr. Senear had been of the opinion that the case was one of dermatitis herpetiformis, but there were only pustules as primary lesions and the others seemed to him to be the result of crusts. There was nothing that usually went to constitute the multiformity in dermatitis herpetiformis, and after listening to Dr. Wile's remarks he thought the diagnosis of pemphigus should be considered.

Dr. Eisenstaedt thought the diagnosis of true pemphigus might be established. He had noticed the things brought out by Dr. Wile.

Dr. Norman Walker thought after a single examination, the case should not be called dermatitis herpetiformis. The man had no itching, the distribution was not so much on the shoulders as was usually found in dermatitis herpetiformis and there was a striking absence of the pigmented rings usually seen. He would not care to register a diagnosis of dermatitis herpetiformis without further observation.

Dr. Oliver stated that he had first seen the patient four days previously. At that time some of the lesions were vesicular and later the lesions became bullous. The patient did have itching, although he said he did not, and continually asked for lotions to relieve the itching. He had thought of pemphigus but on the whole thought dermatitis herpetiformis should be considered more probable.

ULCERATING SYPHILODERM WITH NEPHRITIS. Presented by Drs. Ormsby and Mitchell.

A man, aged 24, with a negative history previous to the present disorder, had lesions which had been appearing, healing, disappearing and reappearing over a period of six years, and had attacked at various times the scalp, neck, face, upper and lower extremities and the trunk. At the time of presentation there were many scars and active lesions. The ulcers varied in size from that of a silver half-dollar to four times that size and were crust covered, many presenting a rupial appearance. The edges were well defined but only slightly indurated. The scars were smooth, white, thin, shining, slightly depressed, and occurred in patches made up of individual smaller lesions. The urine contained a large amount of albumin and casts, the latter being chiefly granular. The Wassermann reaction was negative.

DISCUSSION

Drs. Irvine and Potthoff thought it was blastomycosis.

Dr. Zeisler said the lesions looked to him like blastomycosis, but Dr. Ormsby said no organisms had been found, so the case was probably one of tertiary syphilis.

Dr. Stillians thought it was blastomycosis but it might be an ecthymatous eruption in a man with lowered resistance.

Dr. Norman Walker said he had not had a great opportunity to see cases of blastomycosis, but the scars suggested syphilis rather than blastomycosis.

Dr. Quinn said that the first cases of blastomycosis he saw were seen with Drs. Hyde and Montgomery and they greatly resembled the scars of late syphilis.

Dr. Ormsby said the scars of blastomycosis were something like those of syphilis, but the entire scar in this case was made up of a group of smaller scars, which was typical of syphilis and not of blastomycosis. The man presented a superficial late syphiloderm of a type which used to be seen frequently, but was rarely seen now; a type, also, which was very resistant to treatment. He had seen such patients who had to be cared for for many months and kept in bed. The cases responded very slowly to the old methods of treatment. This man had improved considerably under arsphenamin; he had received five injections, the first only 0.2 gm., and the second 0.3 gm. Dr. Ormsby was not at all sure that the nephritis was syphilitic; if he were, he would be more heroic as to treatment. The patient had now been under observation for two days and he would be placed in the hospital and tested out. There was no doubt in his mind that the case was syphilis but the Wassermann reaction had always been negative.

Dr. Wile asked whether it had not been Dr. Ormsby's experience that cachectic individuals with severe syphilis frequently had negative Wassermann reactions. He had under his care at the present time a patient whose body was covered with scars of an extensive rupial syphilid and whose Wassermann reaction had uniformly been negative. Within the past year he had seen a second case in which an indubitable diagnosis of syphilis of a malignant type in a cachectic individual was maintained in spite of the absence of a positive Wassermann reaction. It seemed as if in these severe cases there was no reaction on the part of the patient to the infection and no antibodies were produced. It was not impossible that the albuminuria present in Dr. Ormsby's case was part of the syphilitic process. Early syphilitic nephritis is a fulminant type and characterized by enormous albuminuria; casts are not a striking feature of the urinary picture. Dr. Wile suggested that if the albumin content was very high it would be presumptive evidence that the nephritis was syphilitic. It must be remembered, however, that the more chronic type of nephritis can also occur associated with the later stages of syphilis.

Dr. Ormsby stated that the albuminuria was chronic but not excessive, and the casts were quite abundant. About four years ago they had a patient with about 75 per cent., by volume, albumin and within a short time his kidney condition cleared up, as well as the lesions of syphilis, following one injection. This man had received five injections and was improved.

Note.—(July 23, 1920.) A large amount of arsphenamin has been given since the patient was shown, with the result that many of the lesions have healed and the urine has become perfectly normal.

A CASE FOR DIAGNOSIS. Presented by Drs. Ormsby and Mitchell.

A man, aged 32 years, presented a lesion on the lip which had been present for about two months. At first it was an excoriation which developed a new growth and at the time of presentation it was a warty lesion, having changed its type considerably. There was no glandular enlargement.

DISCUSSION

Dr. Michelson believed it was a plain wart on the lip but that it was potentially malignant and should be treated as such.

Dr. Irvine thought that the facts that the lesion was only a few weeks old, and that it was much higher in the center than on the edge, were in favor of a common wart, but he agreed with Dr. Michelson that it should be treated as essentially malignant.

Dr. Ormsby stated that when the man was first seen in the clinic the lesion was much inflamed, and there was no suggestion of its being wart-like at that time, but it had just been painted with iodin. The crust had been removed. The question in his mind then was whether it was a beginning epithelioma or an infection of some sort with which he was not familiar, or a primary lesion of syphilis. His impression at present was that it was a beginning epithelioma. It had bled slightly when the crust was removed.

EPITHELIOMA. Presented by Dr. Zeisler.

A man, aged 60, first came under Dr. Zeisler's care in March, 1920, at which time he presented an ulcerated lesion on the back, about the size of the palm. The patient wore an artificial arm and the lesion began about five years ago at a point where the strap crossed the shoulder. Under radiotherapy it had cleared up markedly, and was now rapidly healing.

DISCUSSION

Dr. Oliver considered the lesion an epithelioma that was healing under treatment.

BLASTOMYCOSIS. Presented by Drs. Ormsby and Mitchell.

A man, aged 36, had suffered with this disorder for twenty years. He lived in a neighboring state and had been treated in various places during this period. The lesions were situated about the anal region, extending over the perineum, involving the scrotum, part of the penis and an area down either side on the surface commonly attacked with eczema marginatum. The lesions were papillomatous areas and scars and a few superficial ulcers. The obstinate career of the disorder and the pain were unusual features. Smears showing the micro-organisms were presented.

BLASTOMYCOSIS. Presented by Dr. Stillians.

In an Italian, chauffeur, aged 45, the disease began in the right arm in 1914, but there had been lesions on the face, back and scrotum since the onset. He had been treated with radiotherapy, neo-arsphenamin and iodids. At the time of presentation he showed scars on the right arm, face and back, the large scar on the back showing a recurrent patch of dermatitis of recent date.

A man, aged 40, presented lesions that had disappeared under arsphenamin and iodid treatment. The lesions had been present for eight months, beginning while the patient was at work in the stock yards. The first lesion appeared on the face under the left eye, spreading rapidly over the entire face, wrists and hands. One lesion was present on the chest. He had received iodid and copper sulphate, without distinct improvement. One injection of 0.6 gm. neo-arsphenamin had proved very beneficial. After a second dose the lesions almost disappeared. Three weeks before presentation they again showed signs of activity; another 0.6 gm. was administered and the lesions disappeared almost entirely. The blastomyces had been demonstrated.

Dr. Norman Walker thanked the members of the society for their courtesy in arranging the meeting so that he could attend, and stated that he had read the society reports with great interest in the past and would do so with added interest in the future. The spirit of camaraderie among the members was very pleasant and he was glad to have an opportunity of being present.

Book Review

SYPHILIS. A TREATISE ON ETIOLOGY, PATHOLOGY, DIAGNOSIS, PROGNOSIS, PROPHYLAXIS AND TREATMENTS. By HENRY H. HAZEN, A.B., M.D. Pp. 646. St. Louis: C. V. Mosby Co., 1919. Price, $7.00.

There is room at present for a treatise that summarizes our present knowledge of syphilis. The study of syphilis has been so intensive in these last few years, so much knowledge is accumulating, so many men who are entitled to be heard are expressing their views on moot points, that we need new synopses of the subject at short intervals, and that man does a service who gives us a good one. Hazen has done this service. He has given us, if not a *magnum opus*, a book that is worthy to be called a treatise on syphilis. The entire subject has been covered, and the work takes on an encyclopedic character from the fact that he has enlisted the cooperation of many authorities who have written on topics with which they are especially familiar.

To enumerate only the chief contributors: Reasoner has written on infection and immunity; Dunlap, on bones, joints, etc.; Fowler, on the male genitourinary organs; Lind, on the central nervous system; Dabney, on the eye; Greene, on the ear; Craig, on the Wassermann reaction, and Schamberg, on arsphenamin.

The work is well balanced, and does not fail, as so many works on syphilis fail, in being full on topics with which the author is familiar or interested, and weak on those with which he is not. Of course the large part of the work is by Hazen, and he has taken great pains to give the various topics in full, including the last word on the subjects.

Indeed, if there is a general criticism to be made of the book, it is that it is a syphilographer's book, a scholarly work; for it does not give the precise details and definite instructions about treatment, for instance, that the average physician—not only, the general practitioner but the average man in nearly all of the specialties—needs. But that is not a fair criticism, for what the average physician needs is to have pounded into him the elementary facts of our knowledge of syphilis. He needs a primer, and this is a treatise on syphilis.

The book can also be praised in detail. It is written in good style. The views are orthodox and sane, and restrained on matters of uncertainty. The author is courageous in just criticism, but liberal in his consideration of others' views. Altogether it is a commendable book. Illustrations are abundant. They are well selected and many of them of excellent quality. The printing, paper, and general make-up are first class.

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A CONTRIBUTION TO THE STUDY OF THE ETIOLOGY OF XANTHOMA MULTIPLEX*

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Until recent times speculation as to the origin of xanthoma multiplex concerned itself chiefly with clinical observations of its association with jaundice, hepatic disease and diabetes. Little distinction was drawn between the several clinical types.

LITERATURE ON THE SUBJECT

Thus, Kaposi, in his treatise on skin diseases, stated "Nothing definite is known concerning the causation of this remarkable affection. It has been attributed to hepatic affections because jaundice has been observed in more than half the cases. But it seems probable that the same process of nodular development may attack the liver and thus give rise to jaundice."

Hyde in his textbook on skin diseases, 1900, said: "There is a growing belief that xanthoma is due to embryonic and local causes."

During the past twenty years much study of the histopathology of xanthoma lesions has been made, and at present there is a fair degree of unanimity concerning their histologic peculiarities. These investigations, however, have dealt almost exclusively with the cellular architecture of xanthoma. There have been even remarkably few theoretical views about the affection beyond the discussion of peculiar cutaneous tumors.

Consideration of the pathology of zanthoma lesions has resolved principally about the question of a tumor of local origin or one due to secondary inflammatory irritation.

Virchow thought that the process is a connective tissue neoplasm accompanied by a deposit of fat or by fatty degeneration. Touton and

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[*] Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

[*] Rosenbloom, J.: The Cholesterol and Cholesterol-Ester Content of the Blood in Xanthoma Tuberosum Multiplex, Arch. Int. Med. **12**:395, 1913. Method of Windhaus.

Kobner thought that it is an endothelioma; while Hallopeau and Ehrmann deduced xanthoma to be of embryonic origin analogous to the nevi.

Various observers are now quite well agreed concerning essential facts, but there is divergence of opinion as to whether the process is primarily an inflammatory one or a local tumor of probable embryonic origin.

Pollitzer,[1] who has made a thorough study of the histopathology of xanthoma, classifies xanthoma multiplex and xanthoma palpebrarum as two separate conditions. The peculiarities of the former he ascribes to fatty degeneration of the orbicularis muscle, while the latter variety he regards as a secondary connective tissue hyperplasia.

Pinkus and Pick,[2] in 1908, made studies of xanthoma palpebrarum, xanthoma tuberosum and xanthoma diabeticorum. They found each of these types were composed of the same cellular elements, and they considered them to be "microchemically and microphysically identical." They concluded that the peculiar substance of xanthoma is not fat but a cholesterol-ester, a material supposed to be found in the blood in icterus and diabetes in increased amounts, and that its deposition in the tissues produces the formation of xanthoma.

Pringsheim,[3] in the same year, examined xanthoma tissue of the skin and found certain acetone-soluble crystals present which gave all the reactions peculiar to cholesterol. He believed this substance to be the same as that described by Pinkus and Pick and he thought that the substance (cholesterol) is deposited in xanthoma lesions from the blood.

Chauffard and Laroche,[4] in 1913, claimed that xanthoma is probably caused by an increase of the cholesterol content of the blood serum. He inferred that it is a sign of lipolytic insufficiency of the pancreas and is to be regarded less as a tumor than as a local reaction of the skin to cholesterol present in the blood.

Pollitzer and Wile, in 1912, described infiltration of the perivascular and intercellular lymph spaces in xanthoma lesions with a fatty substance which is present also in newly formed cells. Xanthoma giant cells—on staining with osmic acid—were found to be entirely filled with this substance. These observers reasoned that xanthoma tuberosum represents "an irritative connective tissue hyperplasia in which the extravasation of cholesterol fatty-acid-ester, present in excess in the blood, serves as the stimulus. These observers also stated that

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1. Pollitzer: New York M. J. **2**:73, 1899.
2. Pinkus and Pick: Deutsch. med. Wchnschr. **34**:1246, 1908.
3. Pringsheim: Deutsch. med. Wchnschr. **34**:2145, 1908.
4. Chauffard and Laroche: Centralbl. f. Biochem. **13**:102, 1912.
5. Pollitzer and Wile: J. Cutan. Dis. **30**:235, 1912.

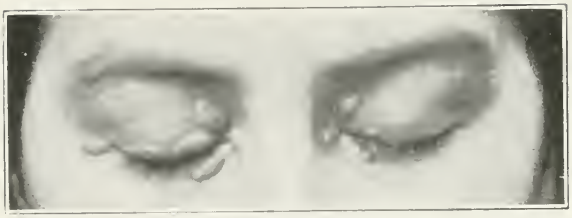

Fig. 1.—Xanthoma multiplex lesions on eyelids.

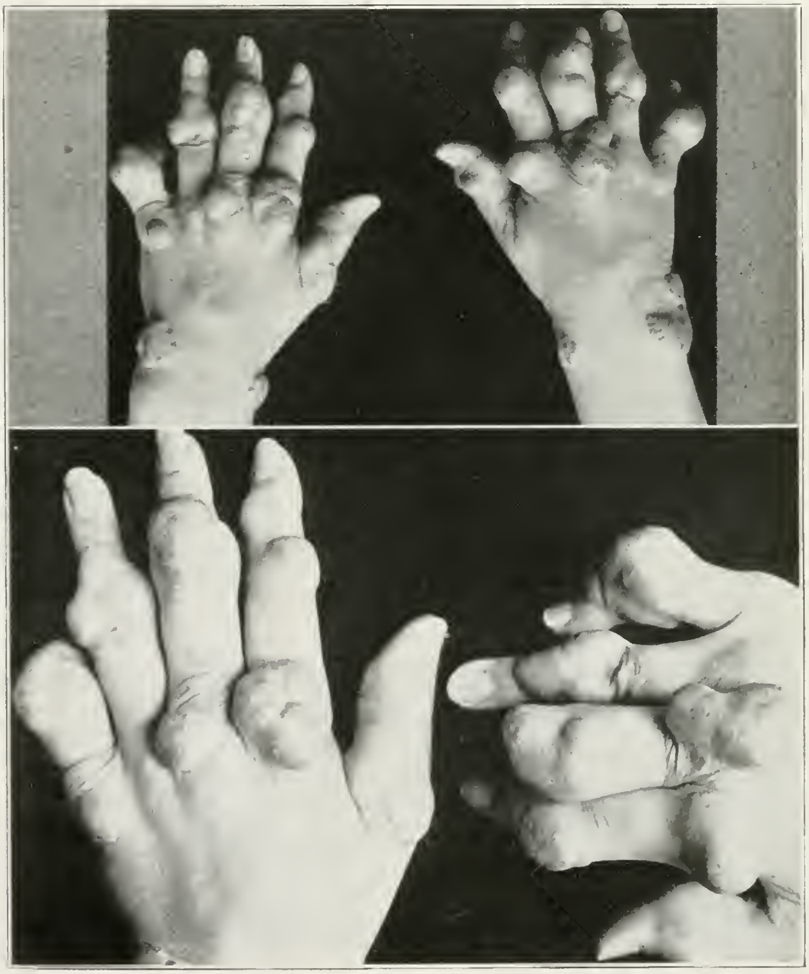

Fig. 2.—Tubercles of hands.

"it is this particular lipoid which it has been demonstrated constitutes the greater portion of the fatty substance in the cells of xanthoma tuberosum."

As it is not definitely stated by Pollitzer and Wile that examination for cholesterol was made from tissue in their case, one may be a little in doubt as to whether their inferences were based on previously reported cholesterol findings, supported by their histologic studies.

Review of the literature respecting the present opinion on the origin of xanthoma multiplex, therefore, shows existing differences. The views held are based mainly on the pathologic examination of skin tissue. Detection of cholesterol as the lipoid material present in the tumors from several cases of xanthoma has led to renewed interest in the subject with advancement of the theory that the cholesterol present in xanthoma lesions is deposited there from the blood in which it exists in excess.

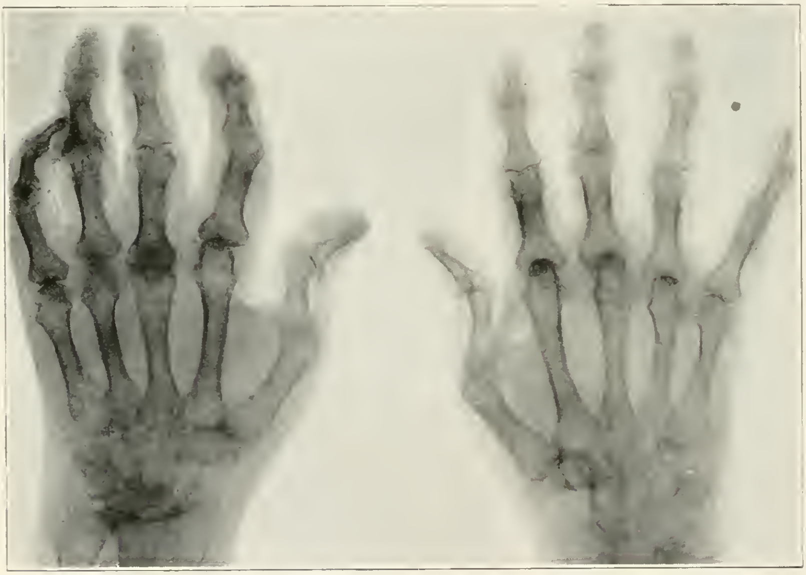

Fig. 3.—Gouty lesions of phalanges; blood uric acid increased.

So far as I have been able to discover, Rosenbloom,[6] in 1913, is the only investigator who has reported the results of examination of the cholesterol content of the blood in a case of xanthoma multiplex. Rosenbloom examined blood for cholesterol from a patient in the clinic of Dr. George H. Fox. He concluded "that in the case studied there was no increase in the amount of cholesterol in the corpuscles and plasma when compared with a normal control."

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[6] Rosenbloom: Arch. Int. Med. **2**:395, 1913.

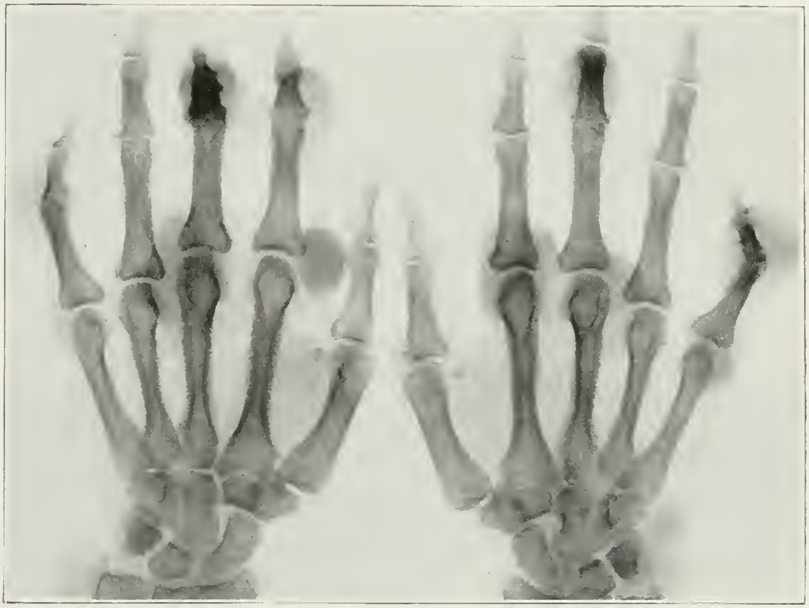

Fig. 4.—Gouty lesions of phalanges; blood uric acid increased.

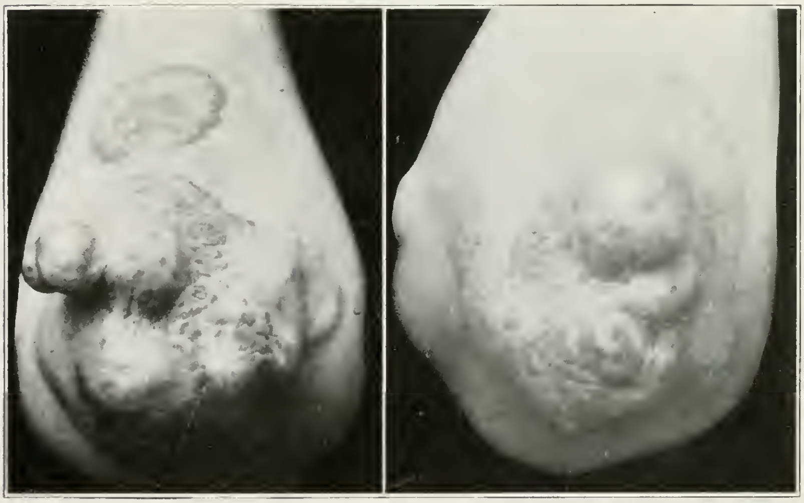

Fig. 5.—Lesions at elbows.

My purpose is to report the results of an examination of the cholesterol content in the tissue and blood from a case of xanthoma multiplex and to refer to the interesting features of a prominent example of this rare dermatosis.

REPORT OF CASE

Family History.—The patient was a woman, aged 27 years; single, a housekeeper, born in Canada of French Canadian parents. She was a resident of Massachusetts. There was no antecedent history of xanthoma in the family except in one brother who developed the affection at 10 years of age. He had the disease until he was 21 years old, when he died as the result of an accident. There was no history of jaundice, diabetes, cancer, or tuberculosis in the family.

Past History.—The patient was said to have rheumatic fever at 12 years of age. Since childhood she had had occasional attacks of indigestion accompanied by headache. She had no remembrance of having had jaundice. An attack of diphtheria occurred at 7 years of age.

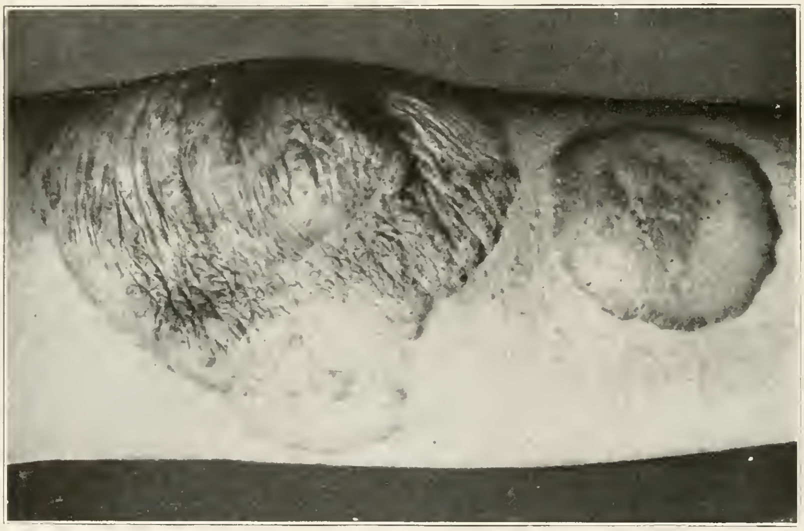

Fig. 6.—Lesions on elbow.

Present Illness.—The patient's mother told her that the present affection began soon after the attack of diphtheria when 7 years old. Lesions appeared first over the knees and extensor surfaces of the phalangeal joints. The initial lesions grew larger and from time to time new ones appeared over various parts of the body and limbs. After a period of twenty years they attained the existing degree of development and distribution.

Skin Lesions.—There was a generalized eruption of tubercles of various sizes over the arms, legs, feet, gluteal region, eyelids and chin. They were quite symmetrically disseminated, predominated on the extensor surfaces and, with the exception of the buttocks, the trunk was practically free from the outbreak. The chief clinical features of the eruption are plane and tuberose elements, the former predominating where the skin is thick and rich in subcutaneous tissue, such as the gluteal region and the flexor surfaces of the arms and legs; while the latter kind occur usually over the extensor surfaces of joints.

While the skin lesions are all of one general class, namely, the tubercle, they may be described as of five kinds: (1) palpebral lesions, (2) nodules appearing over the joints, firm in consistence and covered by pigmented epidermis, (3) flat nodules, of softer consistency and also covered with pigmented epidermis, (4) large plaques of the texture and color of the kinds just mentioned, and (5) hard tumors, occurring over the bones and seemingly attached to them. These are covered by skin of normal color.

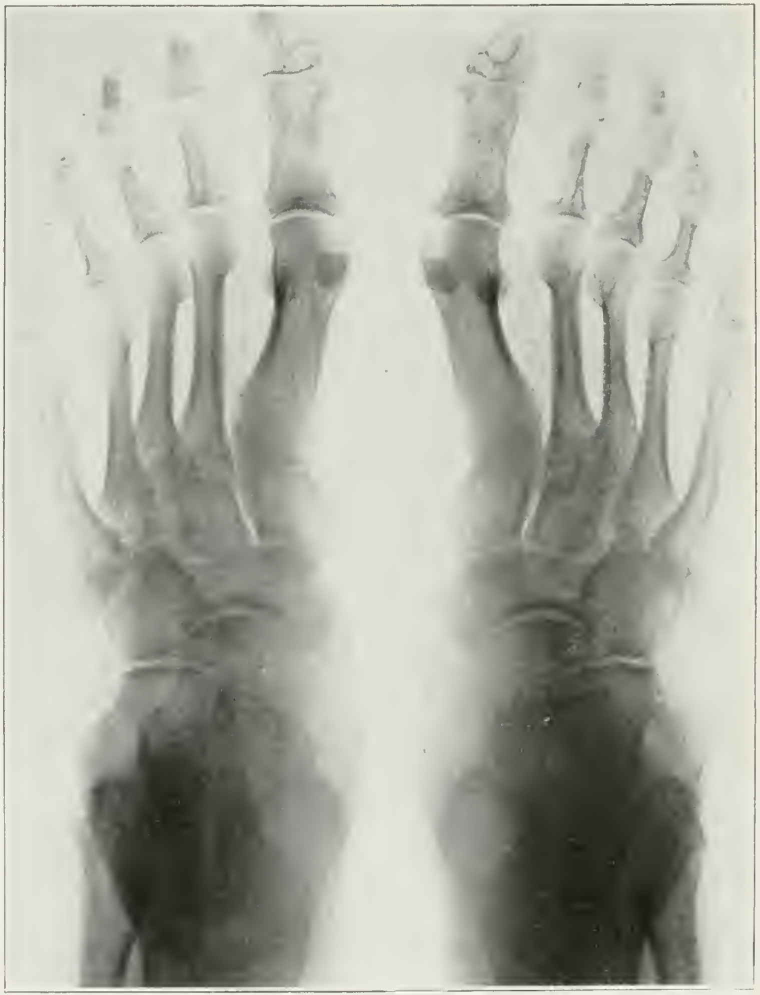

Fig. 7.—Gouty lesions of phalanges; blood uric acid increased.

1. The nodules on the eyelids were soft, of pinkish yellow color, round or oval in shape, smooth, sharply defined and raised from 1 to 2 mm. above the sur-

rounding surface, answering the textbook description of being like pieces of chamois skin implanted in the skin. They vary in size from 4 by 4 to 4 by 10 mm. There were three on the upper right lid, one on the lower lid and one at each canthus of the right eye. Around the left eye there were two on the upper lid, one on the lower and one at the inner canthus.

2. The nodules around the joints were distinctly elevated, moderately firm in consistency, salmon red in hue, freely movable and had a tendency to be lobulated. The epidermis was movable over the underlying tumors. On the hands their arrangement showed decided symmetry on the extensor surfaces at all the articulations between the first and second phalanges and at the metacarpophalangeal joints of the index and middle fingers. At the elbows the nodules were large, hard and freely movable and on the elbow two were attached by a small pedicle of loose skin. On the feet the lesions occurred on the medial surfaces of the great toes, over the articulations of the three outer toes and on the metatarsal joint of the fifth toe.

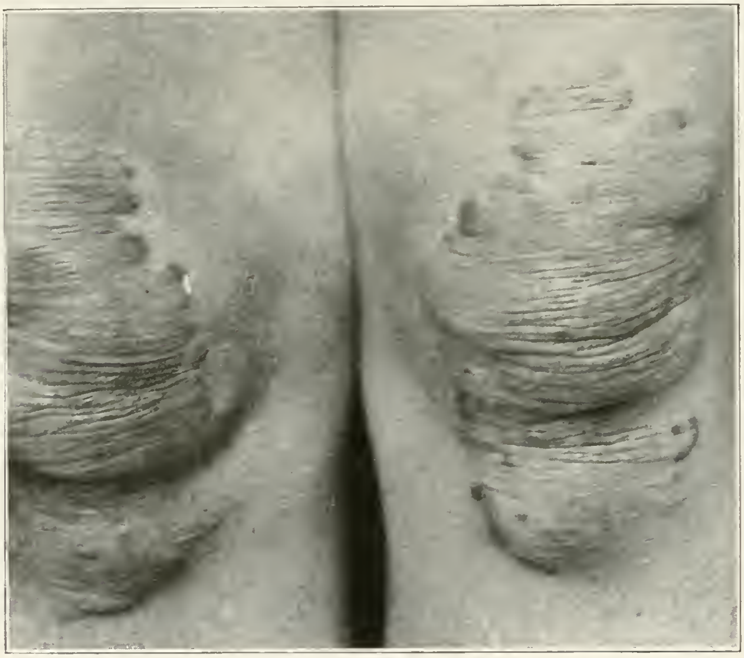

Fig. 8.—Lesions on knees.

3. The plane nodules were in general rounded, salmon pink in hue, soft in texture, elevated from 2 to 4 mm., somewhat irregular in outline and roughened on the surface. The borders were sharply defined. They varied from 1 to 4 cm. in diameter. The centers were often depressed. Coalescence frequently took place to form plaques 5 by 12 cm. in diameter.

4. Except for size the plaques were like the lesions just described. They attained their largest size over the buttocks, where they measured 12 by 18 cm. Plaques also occurred over the elbows, the knees and in the popliteal spaces.

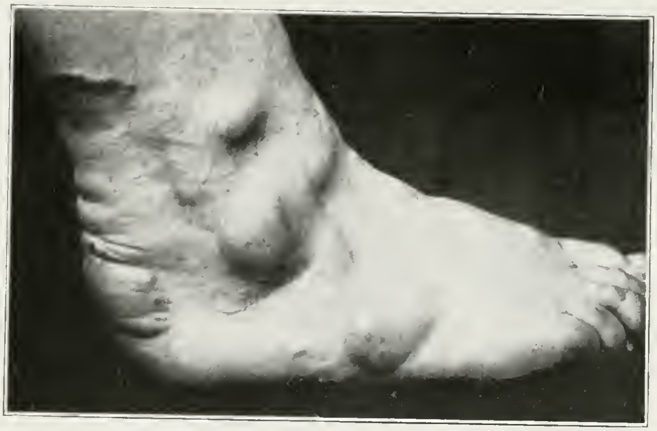

Fig. 9.—Nodules on foot and ankle.

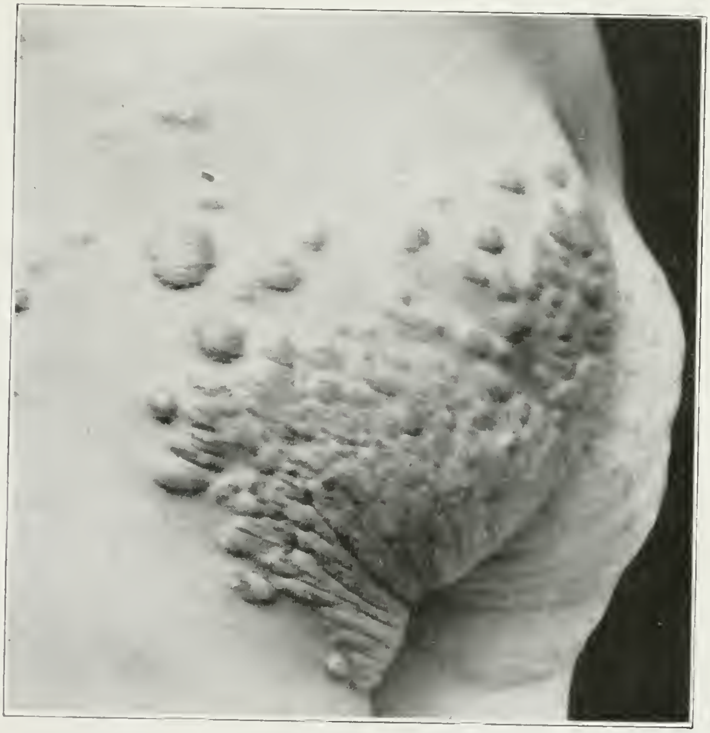

Fig. 10.—Lesions on buttocks.

5. The very hard masses appeared at first like exostosis. They varied in size from 1 by 2 to 3 by 2 cm. and were elevated from 0.5 to 1 cm. above the surface of the bone. In most instances they felt osseous, but in some areas they could be slightly depressed and moved a little. Those over the external malleoli were the hardest and the most difficult to move. Elements of this sort appeared on the backs of the hands, over the anterior surfaces of the tibiae and especially around the ankles where they produced marked deformity. Here they were present, not only over the bony surfaces, but also among the tendons of the leg. On the backs of the hands they moved definitely with the tendons.

Roentgen-ray examination subsequently proved the hard tumors to be of soft tissue and presumably similar in character to the others. Attempts to remove some of the finger nodules by excision also verified the clinical impression that the xanthoma had invaded the tendon sheaths. In fact, the tendons were so much infiltrated by xanthoma tissue that satisfactory correction of the finger deformity by dissection was quite impossible.

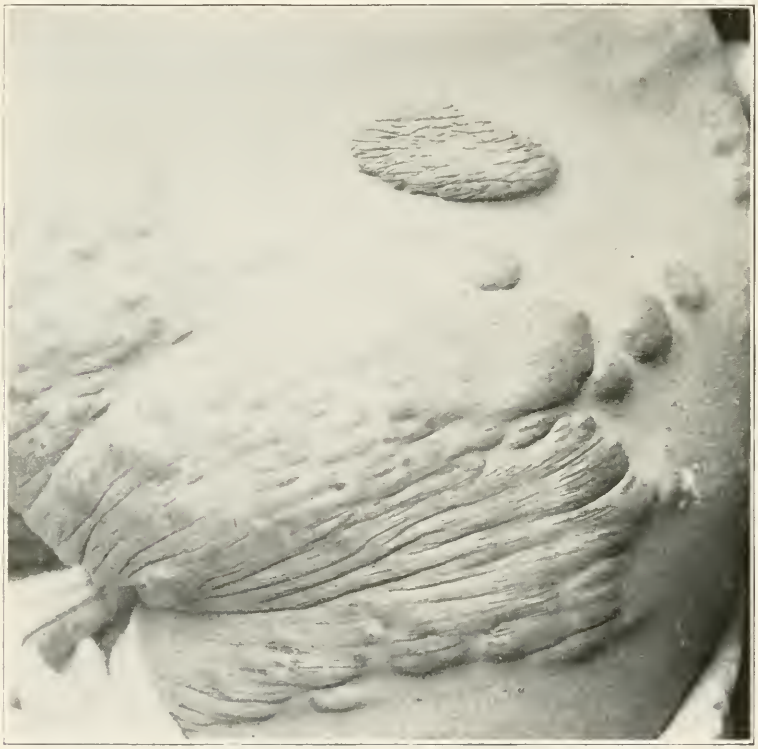

Fig. 11.—Lesions on buttocks.

Physical Examination.—The patient was well developed and nourished. General examination was negative except for the cardiac condition. After much examination and discussion, the heart symptoms may be summarized by quoting the opinion of the consulting physician: "She presents the signs of endocarditis of the mitral and aortic valves. These signs are not entirely typical, e. g., the basal systolic murmur with its transmission especially to the right carotid and

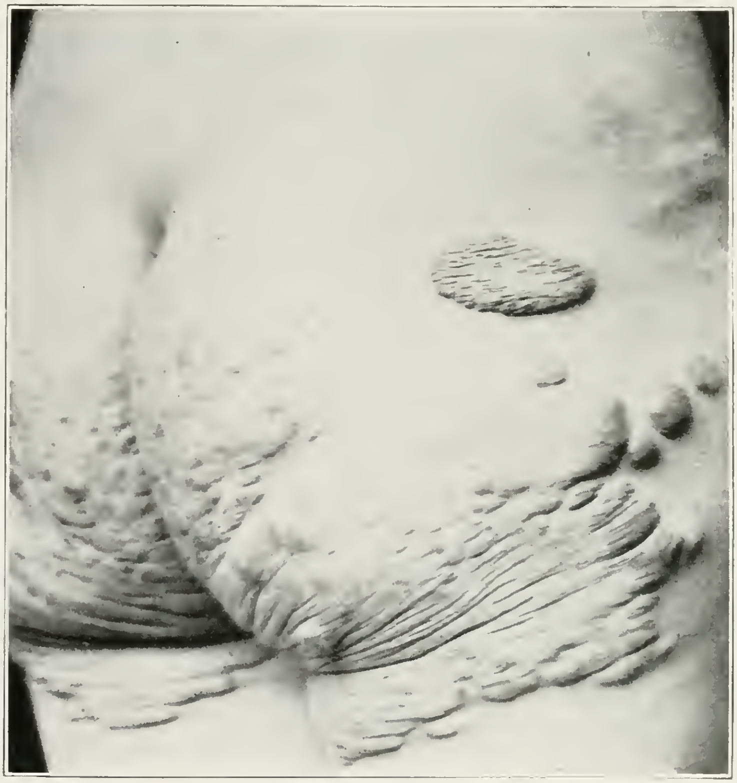

Fig. 12.—Lesions on buttocks.

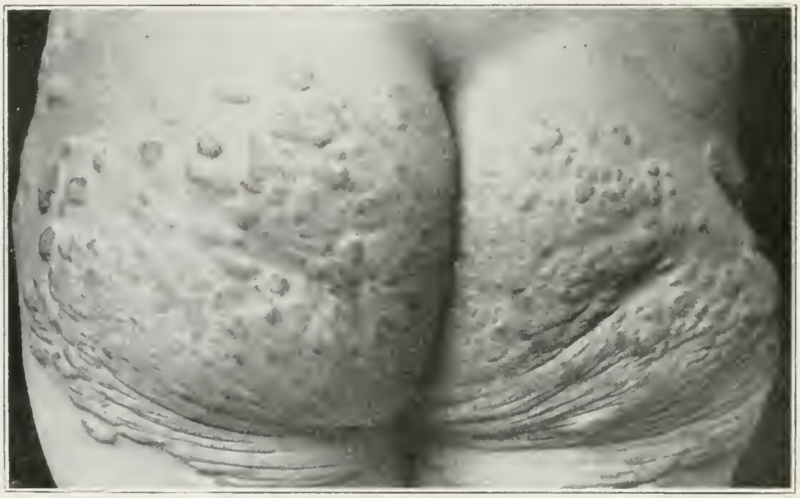

Fig. 13.—Lesions on buttocks.

also the pulsation in the suprasternal notch. Ordinarily such signs would satisfy one, in an adult, as to the presence of endocarditis with chronic deformity of the aortic and mitral valves. There is nothing in the heart examination that is not consistent with xanthomatous deposits in the endocardium and perhaps in the aorta and great vessels. But, of course, this opinion is entirely inferential."

The Wassermann examination was negative. Urine examinations were repeatedly negative; especially as to acetone and bile. The blood count was normal. The blood uric acid was increased (4.3 mg. per 100 c.c.); the blood sugar was 0.091 per cent.

Roentgen-Ray Examination.—This proved the hard masses over the shins and malleoli to be of soft, probably xanthomatous tissue. The roentgen-ray plates also showed gouty lesions of the hands and feet.

Pathologic Examination.—Several of the large and small lesions were excised for histologic and chemical examination.

Histologic Examination: Examination of numerous sections demonstrated the tissue to be a tumor composed of fibroblasts forming a loose network within which were large vacuolated cells containing apparently a fatty material. There were many needle-like spaces between the fibrils which probably contained cholesterin crystals. About these spaces were small clusters of foreign body giant cells. Sections stained with osmic acid showed the presence of fat in the vacuolated cells and in the lymph spaces.

Chemical Examination of Tissue for Cholesterol: Cholesterol was found in large quantities in three of the nodules examined. Unfortunately the quantitative analysis for cholesterol in tissue was not completed at the time of writing, but this estimation, together with further chemical studies on the case, it is planned to report in a subsequent paper.

Examination of Blood for Cholesterol: Blood was obtained from the patient by the usual method for Wassermann tests. In the examination for cholesterol, as well as for fat in the blood, the method of Bloor[7] was employed; the normal variations for which have been standardized by several hundred examinations of normal blood.

Blood was examined under three regimens of diet. Two analyses were made under usual mixed diet, one after a week on low fat diet, and one following a week under high fat diet. In each case the fasting blood (fourteen hours after food) was used. In order to exclude the possibility of acidosis affecting the cholesterol findings, the urine was examined repeatedly for acetone by the delicate Scott-Wilson reagent. At no time did the patient display any clinical symptoms of acidosis.

The wide variation in the quantitative figures between Rosenbloom's results and those in my case are apparent and even startling. Those of Rosenbloom fall below the normal limits as established by Bloor, whose method for the estimation of blood cholesterol and blood fat is the one now accepted and used in the department of biologic chemistry of the Massachusetts General Hospital.

Explanation of these differences has been sought, but the only interpretation of them to be offered lies in the greater delicacy of recent methods used for cholesterol estimation. I am informed by

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[7] Bloor: J. Biol. Chem. **24**:223, 1916; idem. **27**:377, 1914.

Dr. Willey Dennis, chemist at the Massachusetts General Hospital, who has carefully verified all the quantitative estimations given in this paper, that the greater accuracy of procedures for the detection of cholesterol used during the past five years warrants the assumption that quantivation by the method employed is the more accurate.

TABLE 1.—Xanthoma Multiplex: Cholesterol Content in Blood

		Cholesterol	Fat	Alkali Reserve
Jan. 15	Normal diet	660 mg. (0.66%)	2,000 mg. (2%)	
Jan. 18	Normal diet	650 mg. (0.65%)	1,700 mg. (1.7%)	
Jan. 30	Low fat diet	660 mg. (0.66%)	1,400 mg. (1.4%)	
Feb. 7	High fat diet	999 mg. (0.99%)	1,000 mg. (1%)	48.1 volume per cent. normal

Cholesterol content in blood. Fasting blood (14 hours after food).
Normal cholesterol 210 to 240 mg. per 100 c.c. (0.2 per cent.) ⎫ Method of
Normal fat 300 to 400 mg. per 100 c.c. (0.3 per cent.) ⎭ Bloor

TABLE 2.—Cholesterol Content in Blood *

	Blood Corpuscles	
	Cholesterol	Cholesterol-Ester
Xanthoma tuberosum	65 mg. (0.065%)	Trace
Control	68 mg. (0.068%)	Trace
	Blood Plasma	
	Cholesterol	Cholesterol-Ester
Xanthoma tuberosum	48 mg. (0.048%)	22 mg. (0.022%)
Control	46 mg. (0.046%)	28 mg. (0.028%)
	Total Cholesterol Content in Blood	
Xanthoma tuberosum	135 mg.	
Control	142 mg.	

* Rosenbloom, J.: The Cholesterol and Cholesterol-Ester Content of the Blood in Xanthoma Tuberosum Multiplex, Arch. Int. Med. **12**: 395, 1913. Method of Windhaus.

Cases of xanthoma with cardiac symptoms, subsequently proved at necropsy to be due to xanthoma deposits in the endocardium, have been reported by Lychzen and Knauss, Pavy and Fagge and by Noxon. Cranston Low[8] refers to a case of xanthoma in a girl 11 years old, who showed heart symptoms similar to those in the present case. Low's opinion as to probable existing xanthoma of the heart was necessarily inferential, as is my own.

Other cases of xanthoma with cardiac lesions of unproved etiology have been reported by Poenngen, Pollonon, Vidal and Gynne.

SUMMARY

The cholesterol blood content in this case was found to be considerably increased under normal mixed diet, under low fat diet and under high fat diet. Under high fat diet the increase was excessive. Cholesterol was also found in large quantities in all xanthoma lesions examined.

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[8] Low: Brit. J. Dermat. **22**: 109, 1910.

From the findings referred to above it seems probable that xanthoma multiplex is a dermatosis whose origin lies in the increased amount of cholesterol in the blood, the skin lesions of which are caused by its deposition in this tissue where it induces a peculiar secondary connective tissue hyperplasia.[9]

In conclusion, I desire to give full credit to Dr. Willey Dennis, chemist at the Massachusetts General Hospital, for making the chemical examination and to acknowledge to her my thanks for verification of all the quantitative figures submitted.

237 Marlborough Street.

DISCUSSION

Dr. Fordyce said he had recently had a case of extensive xanthoma multiplex in which the cholesterol content in the blood was increased. Although the case clinically was similar to xanthoma diabeticorum, the urine was free from sugar.

Dr. Pollitzer thought it was gratifying to find in this complete report a corroboration of the findings which he and Dr. Wile had advanced some years ago. Dr. Burns agreed that the lesions were the result of an irritative connective tissue hyperplasia, as the result of the deposit of cholesterol fatty-acid-esters in the tissues. He thought this particular feature might now be regarded as established. At the time they made their studies the methods of the determination of cholesterol in the blood were extremely crude. In regard to the variations which had been found in different reports, it is evident that there must be a variation in the normal cholesterol fatty-acid content in the blood. That there was an increase in these cases seemed established, but it did not follow that the lesions would disappear when the cholesterol fatty-acid-esters in the blood were reduced. They might remain long after the true cholesterolemia had ceased to exist. On the other hand, there was probably a certain amount of absorption going on from the lesions back into the blood. This was apparent from the fact that these lesions were found after many years undergoing a spontaneous reduction in size, and in some instances they had been known to disappear. This must be due to absorption back into the blood, so one might find at one time in a given stage of xanthoma tuberosum an excess in the blood during the active stage of this disease; when the disease was stationary and no new lesions were forming, a normal cholesterol content, and later, if absorption took place, there would again be an increase in the cholesterol content. In the case reported by Dr. Burns the increase was approximately 300 per cent. over the normal of two tenths of 1 per cent. on a regulation diet. In his opinion the case presented a further corroboration of the fact that xanthoma tuberosum was a systemic disease due to excess of the cholesterol fatty-acid-esters in the blood. The lesions tend to form about the joints where there is motion—flexion and extension—and at such points there must be alternations in the local tension on the blood vessels, affording opportunities for the chemical elements dissolved in the blood to be forced out rather than at other points where no such pressure-changes existed.

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[9] In addition to the references already given, the following may be of interest:

Knowles: J. Cutan. Dis. **22**:288, 1914.

Dr. Wile expressed his appreciation of Dr. Burns' paper and stated that the association of xanthoma tuberosum and diabetes was undoubtedly due not to the presence of sugar, but to the associated cholesterolemia, which was found in the latter disease. Dr. Wile called attention to another form of peculiar yellow pigmentation that occurred in diabetes frequently at the end stage of the disease, to which attention had first been called by Van Noorden. This peculiar color is found on the palms and soles and occasionally on the face. It seemed likely that this color was due to the deposition of cholesterol associated with the diabetes in the fascia and fat of the regions affected.

Dr. Stokes thought it might be interesting to recall the work of Anitschkow in which he succeeded in artificially inducing the formation of xanthomas in the rabbit by administering large amounts of cholesterol by mouth and then traumatizing the skin. The xanthomas developed only at the sites of trauma.

Dr. Highman said he was about to quote the article referred to by Dr. Stokes. The author fed lecithin to rabbits in great quantities, but until he traumatized the skin he could not produce the formation of xanthoma lesions. After placing setons in the skin they developed, which made it evident that it is necessary to have some local disturbance in the skin before xanthoma develops. The lesions, after placing the setons, were typical in every detail of those of xanthoma.

Dr. Pollitzer said the work of Dr. Hess tended to show that the peculiar yellow color was due to a pigment and not to cholesterol—to a pigment derived from vegetable matter. Diabetic patients are fed largely on green vegetable matter, which contains a large amount of coloring material that has been called carotin from the fact that it is most abundantly found in carrots. It had been found that it was possible to color a baby yellow by feeding it carrots. Dr. Hess had demonstrated this in babies in New York and this discoloration occupied in large part the regions which are called seborrheic, the yellowish tinge appearing notably in the face and in the nasolabial folds. Cessation of the feeding of carotin results in a gradual disappearance of the yellow discoloration, very often with desquamation.

Dr. Burns (closing) said that his paper was presented only as a single observation and he had made no attempt to draw conclusions, since this was probably the first reported case of xanthoma multiplex in which increase of the cholesterin content in the blood was observed.

Dr. Burns thought the observation of the excessive cholesterin content in the blood in cases of xanthoma multiplex ought to be confirmed by further work. In diabetes it was recognized that cholesterol existed in some cases but not in others. The variation in the cholesterol content of the blood in diabetes is enormous, but its relation to the disease is little understood. It may be that xanthoma diabeticorum occurs in the presence of excessive cholesterol, but this view is entirely speculative as little work has been done up to the present time on the relation of xanthoma diabeticorum to this content.

NOTES ON TWO UNUSUAL CASES OF DARIER'S DISEASE

FRED WISE, M.D., AND H. J. PARKHURST, M.D.
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NEW YORK

So many instances of Darier's disease have been recorded in the past thirty years that the mere recital of the symptomatology and description of the histopathologic changes in new cases ceases to be of more than passing interest. All the literature relative to the disease throws not one ray of light on the obscure problem of its etiology; the entire question of causation is as much of an enigma today as it was between 1889 and 1891, when J. C. White, Morrow, Darrier and Thibault published reports of their cases. Referring to its etiology, Jadassohn said that in his opinion the disease belongs in the group of congenital anomalies of cornification, and that it may occur in combination with various anomalies in the same individual, or may occur in the same family. In 1916, Boeck, in demonstrating some patients before the dermatologic congress in Christiania, stated that these individuals are often inferior physically and that they sometimes display evidences of "moral insanity." [1]

Malcolm Morris [2] expressed the opinion that the etiology rests on an endocrine basis, and Strandberg [3] of Stockholm also is strongly in favor of accepting this view, more especially as a working basis for research. The latter directs attention to two points which are at least suggestive: the dystrophic affections of the nails in many of the cases; and the fact that in some instances exacerbations of the eruption have manifested themselves during pregnancy. Macleod [4] published an interesting paper dealing with this subject, calling attention to the fact that Darier himself suggested that this affection was possibly due to a functional insufficiency of the thyroid, but benefit has not so far followed the employment of the remedy in it.

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1. This observation certainly does not accord with my experience. I have seen eight cases, none of which conveyed the impression of being mentally deficient (F. W.).

2. Morris, Malcolm: Internal Secretions in Relation to Dermatology, Brit. M. J. **1**:1037 (May 17) 1913.

3. Strandberg, James: Beitrag zur Frage der Bedeutung der inneren Sekretion in der Dermatologie. Stockholm: Isaac Marcus, 1917.

4. Macleod, J. M. H.: Hormones in Relation to Diseases of the Skin, Practitioner **94**:298 (Feb.) 1915.

Marked advances have, nevertheless, been made in the realm of therapeutics. Radiotherapy can do much toward amelioration of the symptoms; in fact, there is no reason why the judicious employment of roentgen rays should not cure the eruption entirely, with the aid of baths and mild emollient ointments.

The two cases forming the subject of these notes present certain features which we believe of sufficient interest to merit being recorded. Both patients were referred to one of us in private practice.

REPORT OF CASES

CASE 1.—The first was an old man, M. L., whose history was first recorded by Bulkley[5] in 1890 and by Lustgarten and Piffard[6] in 1891. At some period or other of his long career, as a remarkable and striking example of Darier's disease, this patient had graced the offices and clinics of probably all the older dermatologists in this city; and, indeed, he always conveyed the impression of priding himself on the distincton of being the "star case" in the many dermatologic meetings at which he was a subject for demonstration. The first symptoms of the eruption appeared in 1864; he consulted Piffard about 1880 and about ten years later Lustgarten and also Bulkley. One of us (F. W.) saw him in June, 1917, when he was about 75, his disease having existed fifty-three years. At the time of his visit, the eruption was very extensive and the infiltrations in the skin were very pronounced, but the man complained more of annoyance and discomfort than actual itching or sensations of pain. He said that the eruption had changed very little in the preceding twenty years.[7] At the time of this observation, however, a well developed basal cell epithelioma was noted on the right side of the bridge of the nose.

Detailed accounts of this case appear in the papers alluded to and as the lesions had undergone very little change since these papers were published, further description would be superfluous. Piffard's article contains an excellent photomicrograph of sections prepared at the time by Fordyce; the characteristic *corps ronds* are here beautifully illustrated. On looking up the various articles dealing with his case, we were surprised to find that a photographic reproduction of his eruption had been omittted in these publications. This seemed to be all the more remarkable, considering the fact that Lustgarten presented a photograph of the eruption before the tenth international dermatologic congress, which met in Berlin in 1890. The opportunity was therefore taken, at the time of the patient's visit, to obtain a photograph of the eruption as it appeared in 1917. At the same time, a small piece of diseased tissue was removed, to furnish material for further study.

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[5] Bulkley, L. Duncan: Psorospermosis Follicularis Cutis, Med. News (Nov. 8) 1890.

[6] J. Cutan. & Genito-Urin. Dis. **9**:7, 14, 1891.

[7] We were informed by the patient's attending physician, Dr. B. F. Ochs, that he died only recently in New York of pneumonia.

The appended illustrations (Figs. 1, 2, 3 and 4) convey a good idea of the more recent appearances presented by the diseased skin.

A rather interesting feature in connection with the family history is the statement made by Bulkley in 1890 and by Lustgarten in 1891 to the effect that none of the patient's children presented any eruption. Only recently we were informed by Dr. B. F. Ochs that one of the patient's daughters had an eruption of Darier's disease, almost as extensive and severe as that of her father. Disheartened by the unresponsiveness to the many forms of treatment which her father had undergone for so many years, she had steadfastly refused to submit to any attempts at therapy. She died recently, aged about 38, of endocarditis. We were unable to ascertain just when the daughter first exhibited the changes in her skin, but it is evident that her skin was unaffected in childhood, thirty years ago, when Lustgarten presented his paper dealing with her father's malady. This hereditary and familial incidence is, of course, a significant feature of the disease, most of the patients giving a history of the same affection existing in other members of the family.

In striking contrast to the extensive and severe eruption in the foregoing case, our second patient, a young woman, presented what might be termed the opposite extreme: The earliest lesions of the disease, appearing in the form of inconspicuous, widely scattered, rather vaguely defined efflorescences, giving rise to no subjective sensations and constituting nothing more than a cosmetic disturbance. Instead of an eruption which permitted identification at a glance, as in the first case, the lesions in this patient were so far from characteristic that a clinical diagnosis was arrived at only tentatively. Microscopic examination of sections of the lesions was necessary to establish the diagnosis of Darier's disease. An interesting feature in this case was the coexistencce of distinct spots of macular atrophy on the chests and breasts, intermingled with numerous *lineae atrophicae* (vergetures) in the same and in neighboring areas of the skin. The coexistence of Darier's disease and atrophia maculosa cutis has not, so far as we are aware, been recorded before.

According to Darier, "so-called abortive or incomplete cases are not very uncommon." Only recently a case of this kind was described from the Vanderbilt Clinic by Scheer.[8]

Case 2.—Miss J. Z., aged 21, was referred to us March 11, 1920, for consultation. The family and personal histories were entirely negative. No other member of the family, immediate or remote, had, so far as she knew, been afflicted with any skin disease.

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8. Scheer, Max: A Case of Darier's Disease in Its Early Stages, J. Cutan. Dis. **34**:837 (Dec.) 1916.

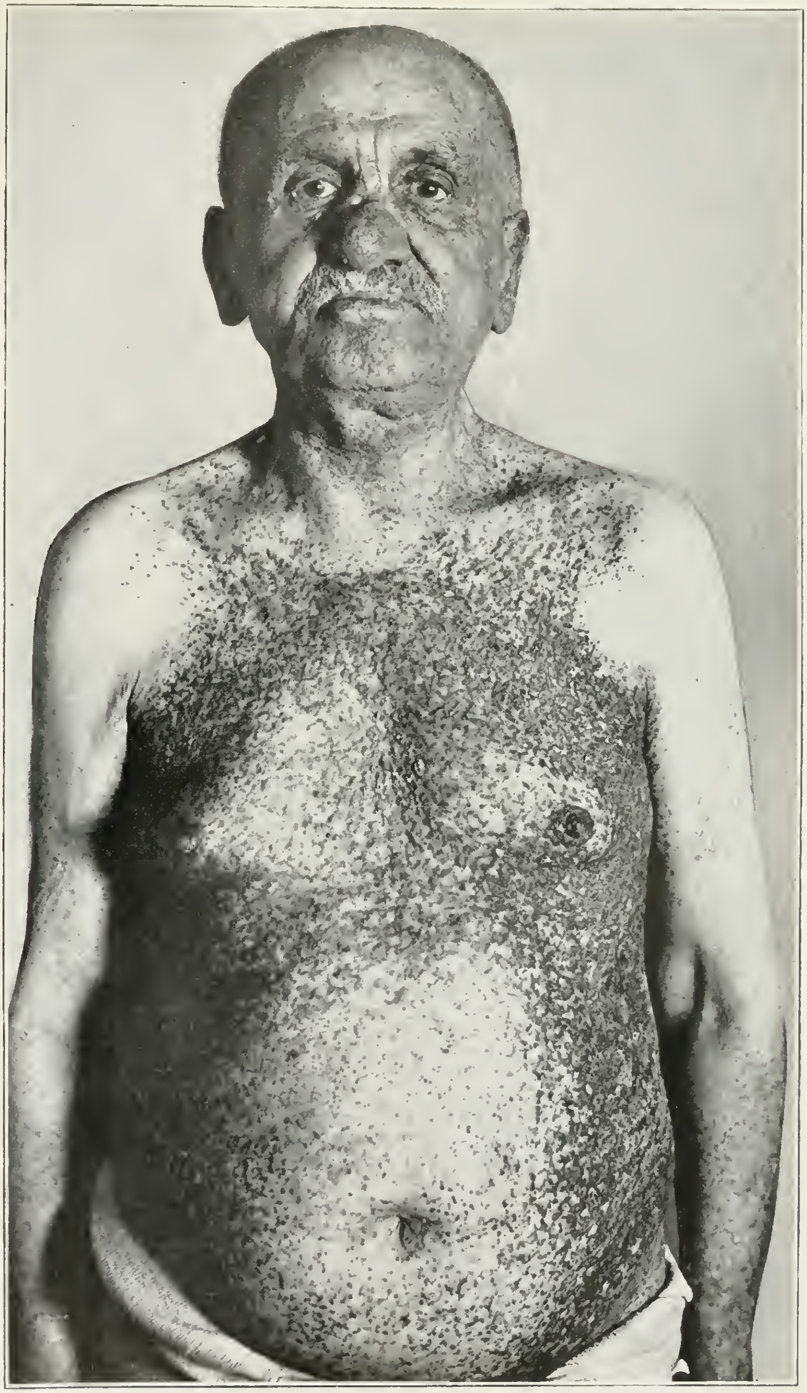

Fig. 1 (Case 1).—Psorospermosis follicularis vegetans (Darier's disease), showing the eruption on the anterior aspect of the body and the site of a basal cell epithelioma at the bridge of the nose.

Physical Examination.—This revealed no other abnormalities than the eruption on the skin, with the exception of obesity, the weight being about 175 pounds; she was of average height for her age. With the object of trying to discover if there might be some obscure disturbance of the glands of internal secretion, the girl was referred for consultation to Dr. Walter Timme, to whom we are greatly indebted for his painstaking examination, directed chiefly toward endocrine changes. Dr. Timme reported negative findings; physical examination, chemical examination of the blood, as well as radiographic examination of the sella turcica failed to reveal the slightest abnormalities. The patient stated that she had always been in good health.

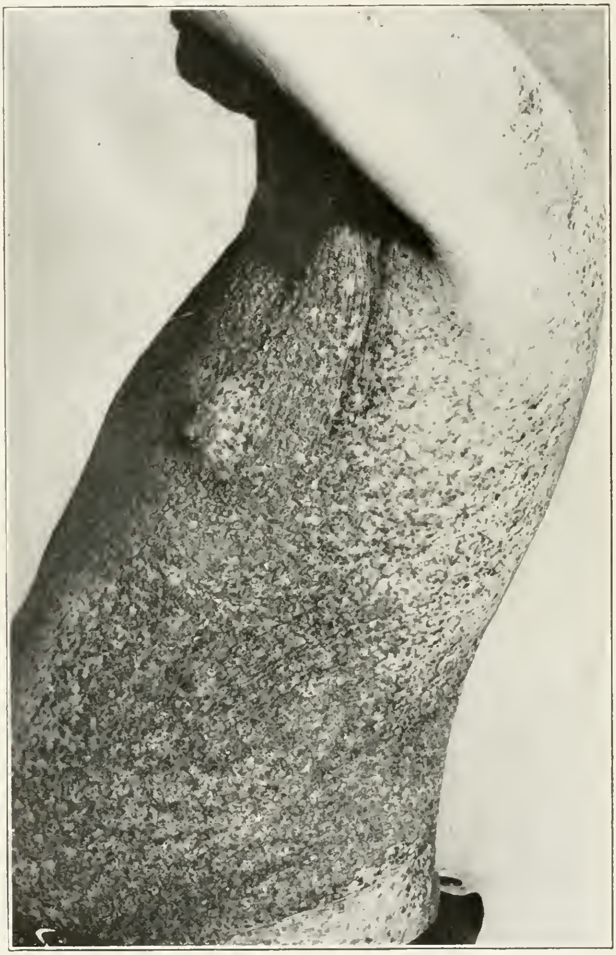

Fig. 2 (Case 1.)—Psorospermosis follicularis vegetans (Darier's disease), showing the eruption on the lateral aspect of the trunk and arm.

The skin of the patient exhibited two entirely different types of eruption (Figs. 5 and 6). In the axillae, on the back and on various areas of the chest and breasts, there was a variety of efflorescences, nearly all of which were follicular and more or less elevated and hyperkeratotic; these were the elementary lesions of Darier's disease. On the anterior surfaces of both breasts, from about the level of the nipples to the clavicles, as well as on both sides and the front of the neck, there were many dime-sized, round and oval, faintly scaly, very slightly depressed macular areas, which glistened slightly when viewed in oblique light; intermingled with these, in the same areas, there were numerous pearly-white, somewhat depressed parallel bands running up and down both breasts and radiating into the armpits and toward the neck and shoulders. These patches and bands were quite typical lesions of atrophia maculosa cutis and lineae atrophicae.

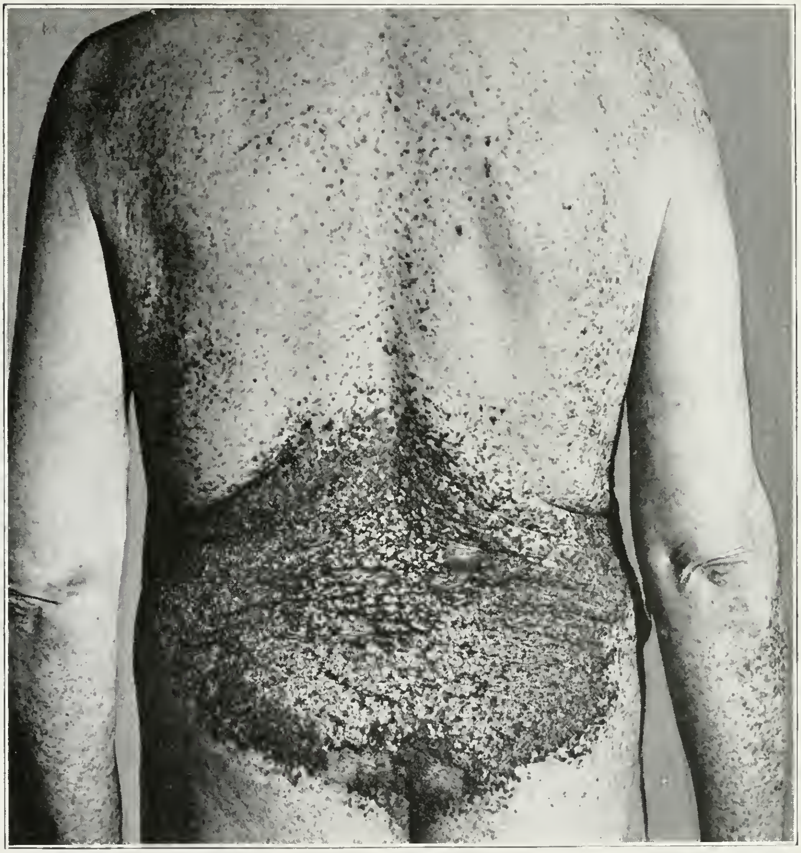

Fig. 3 (Case 1).—Psorospermosis follicularis vegetans (Darier's disease), showing the eruption on the posterior aspect of the trunk.

The lesions of Darier's disease were most pronounced in the armpits. Here they formed dark brown rounded patches of closely aggregated, short, filiform, wart-like protuberances, rather soft to the touch and of a shaggy appearance. The axillary hair was sparse. The clinical appearance of these axillary lesions so closely simulated that of acanthosis nigricans[9] that the differential diagnosis hung in the balance until sections of the skin were examined. The greater part of the mid-portion of the back exhibited many scattered and confluent follicular hyperkeratoses, most of them the size of a pin-head and capped by a tiny scale. In some places the confluence of these follicular lesions produced small patches of irregularly shaped, dark brown, somewhat crusted lesions, the crust being greasy and readily detachable. Similar but less abundant follicular keratotic elements were also present on the anterior surfaces and between the breasts, and a few were scattered over the skin of the abdomen. There were no lesions anywhere below the waist-line, nor on the face, scalp and upper extremities. (The small crust-covered spot on the back, Fig. 6, is a biopsy wound.)

The macular and linear atrophic changes have in part been described; the illustration (Fig. 5) shows the atrophic bands on the breast and the rugose patch of Darier's disease in the armpit. Numerous atrophic striae are seen traversing this patch in various directions.

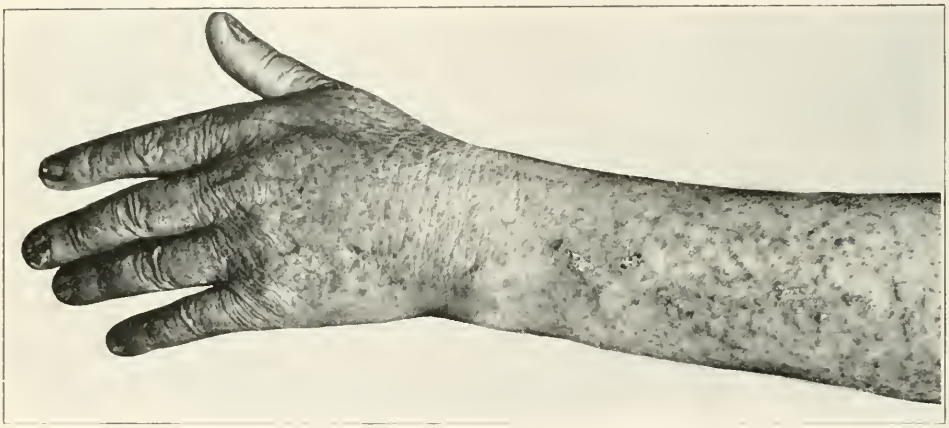

Fig. 4 (Case 1).—Psorospermosis follicularis vegetans (Darier's disease), showing the warty and crusted lesions on the back of the left forearm and hand, and the distrophy of the nails.

The patient first noticed thickening and discoloration of the skin of the armpits about eight years ago, when she was 13 years old. The follicular keratoses of the trunk followed several months after the appearance of the axillary lesions, and slowly increased in number and extent. The atrophic bands and oval lesions were first noticed on the neck and breasts three years ago. The girl had been quite stout since early childhood; there had been no sudden variation in the amount of fat underlying the skin of the neck and chest.

Histopathology.—A small piece of tissue was taken from the armpit for microscopic examination. The section presented a hyperkeratotic epidermis of irregular outline; the papillae were hypertrophied and thrown into folds, the rete pegs being long and narrow, and their cells edematous. Parakeratosis was absent. The follicles were distinctly dilated, some of them filled with horny masses. In the corium, the lymph spaces were distinctly dilated; the collagen was edematous. There was moderate edema of the walls of the blood vessels, with a sparse infiltration of small round cells, fibroblasts and a few epithelioid cells.

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[9] We had the opportunity of comparing the axillary lesions of acanthosis nigricans with these similarly situated patches of Darier's disease, and were unable to tell them apart by the naked eye; even palpation revealed no differences.

Although two or three refractile round bodies were demonstrable in various parts of the epidermal layer, the characteristic *corps ronds* or "psorosperms" of Darier's disease could not be positively identified. Another section was therefore removed, this time from the skin of the lumbar region of the back. This section consisted of nothing more than a few follicular keratotic papules the size of a pin head, evidently the earliest visible lesion of the disease, clinically indistinguishable from ordinary keratosis pilaris. In this specimen the microscopic changes were practically the same as those just described, excepting that the horny layer was much thicker than that of the first section and the collagenous tissue in the pars papillaris was more edematous and took the stain poorly. The rete contained many vacuolated cells, some of them containing granular

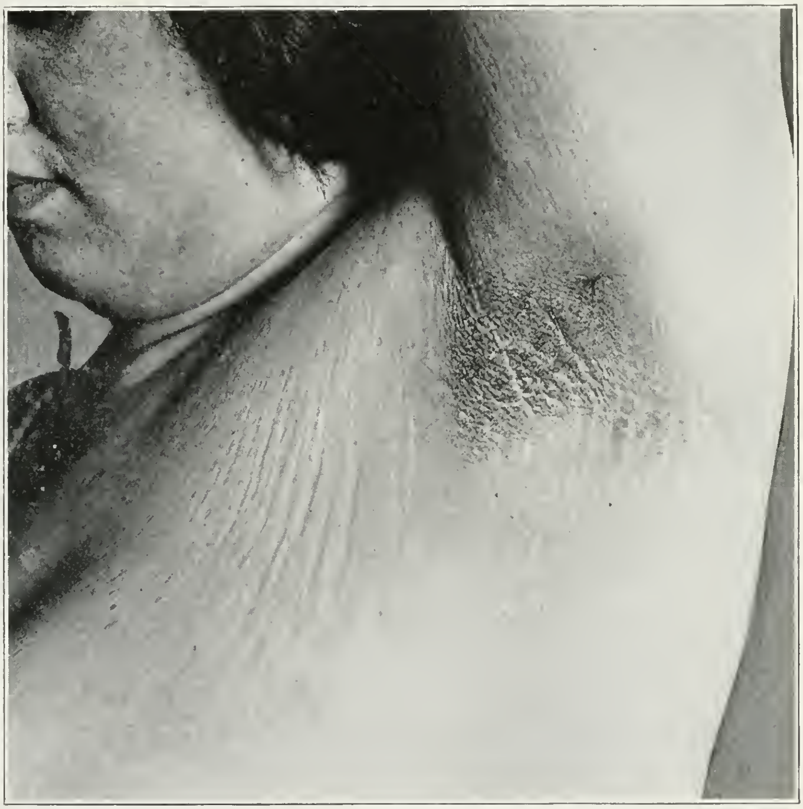

Fig. 5 (Case 2).—Psorospermosis follicularis vegetans (Darier's disease), showing the rugose vegetations in the armpit and the striae atrophicae and macular atrophic spots on the breast and in the axilla.

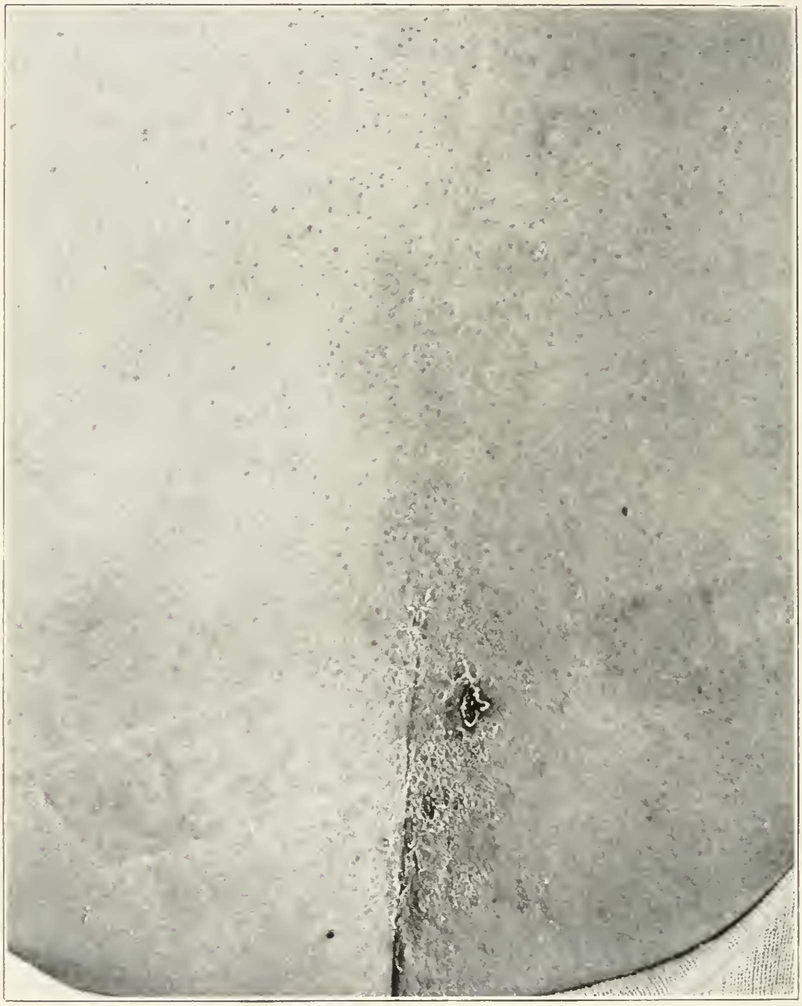

Fig. 6 (Case 2).—Psorospermosis follicularis vegetans (Darier's disease), showing the early follicular keratotic lesions on the back, both isolated and confluent, the latter crusted. The dark crusted lesion to the right of the median line is a biopsy wound.

bodies, others showing deformed and shrunken nuclei; here and there, chiefly in the upper layers of the rete, were seen isolated and grouped round refractile bodies with well defined limiting membranes—the *corps ronds.*[10]

Treatment.—Boric acid ointment was prescribed to anoint the affected regions of the skin, and to retard the formation of scales and crusts. At the same time, roentgen ray treatment was applied to the lesions on the chest, back and in the armpits, in ¼ H. unit doses (skin distance), once in two weeks. After six such treatments, all the lesions of Darier's disease, save those in the axillae, had entirely disappeared, leaving no trace; at the present moment (the patient being still under treatment) the armpit patches show 75 per cent. improvement. The patient was particularly perturbed about the macular and linear atrophic lesions on the chest, neck and upper portions of the breasts, these areas being more or less exposed in the wearing of summer apparel. We informed her that we feared little could be done toward remedying these defects—that they were probably incurable. We were gratified as well as astonished, therefore, to find that both the linear and macular lesions faded away completely in all regions exposed to the roentgen ray, so that today the skin appears to be quite normal in every respect. The patient also received one-tenth grain of thyroid gland extract three times a day. Whether or not this medication had any direct or indirect bearing on the cure of the atrophic lesions, or whether their disappearance may be attributed to the influence of the roentgen rays alone, administered to the follicular keratoses occupying the same fields of the integument, we have as yet been unable to decide. Perhaps the combination of roentgen rays, thyroid extract and massage produced the unexpected result.

To judge from the rapid disappearance of the lesions of Darier's disease on the trunk, it is safe to anticipate a complete restitution to normal conditions, with respect to the remaining keratotic formations in the armpits, after a few additional roentgen ray treatments.

COMMENT

These two examples of Darier's disease are briefly recorded with the realization that, although nothing new is brought out regarding our knowledge of the disease, they at least possess certain features of peculiar interest to the dermatologist, aside from being mere case reports. Viewed from the morphologic standpoint alone, comparison of the two eruptions offers a fascinating clinical study: In the old man it is interesting to note the almost universal integumentary changes, their development and persistence over a period of more than half a century, their recalcitrance to many forms of treatment, and the occurrence of an epithelioma of the face, presumably at the site of one or more follicular keratoses. Compare these to the picture presented by the young woman: an inconspicuous, rather ill-defined eruption of isolated and irregularly grouped follicular keratoses on portions of the chest and back, of eight years' duration, together with more pronounced hyperkeratotic formations in the armpits, the coincidence of macular and linear atrophic lesions of the same fields of skin, and finally, the good results obtained by radiotherapy.

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[10] Drs. Fordyce and Pollitzer, who kindly examined these sections for us, confirmed the microscopic findings.

To revert to the question of etiology: In recent years the impression has grown among internists and dermatologists, that the rôle of the ductless gland secretions cannot be ignored in the search for the pathogenesis of certain obscure skin diseases, more especially with regard to certain atrophies, dyskeratoses and anomalies of cornification. Attention has been especially directed toward such affections as ichthyosis, mal de Meleda, Darier's disease, scleroderma, atrophoderma, trophic diseases of the nails, Raynaud's disease, and others. Osler, Malcolm Morris, Macleod, Johnston, Strandberg, Weiss, Foerster, McEwen and many others have contributed to the literature on this phase of dermatotherapy. The therapeutic results have thus far been meager, but, in a few instances, they have been at least sufficiently encouraging to justify the undertaking of careful investigations of possible *endocrine* changes in patients affected with these several ailments, together with the institution of a rational therapy where indicated. He who reads the transactions of dermatologic society meetings will find that discussions concerning the ductless glands and their relation to the pathogenesis of some skin diseases are becoming more and more frequent. It is true that not all of these discussions attain the high standard of logical argument demanded by science; oftentimes they are tinged with facetious, cynical, even acrimonious periods, which, though amusing to the listener, are in no way helpful to those who are groping in the dark in the search for facts. In the field of research work, nothing can be gained by such crude subterfuges. The whole subject of endocrinology in the realm of dermatology is as yet deeply shrouded in a veil of obscurity; every phase of it must be approached with an open and receptive mind, if the wheat of certainty is to be separated from the chaff of conjecture.

The writers are greatly indebted to Dr. Geo. M. MacKee for the photographs, and to the staff of the pathologic department of Prof. Fordyce's clinic for the microscopic sections.

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LUPUS ERYTHEMATOSUS AND FOCAL INFECTION *

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REPORT OF A CASE

Mrs. B., 35 years old, was referred to me in May, 1918, for the treatment of an erythematous lupus of one year's duration. The eruption, while presenting a wholly characteristic appearance, was distributed over an unusually large area; coin-sized and smaller patches were scattered over the cheeks, the upper and lower lids, behind the ears, in the scalp, on the upper chest, the arms and forearms and in the interscapular region. Some of the larger patches, especially those on the malar eminences, the upper lids and the back, were decidedly thicker and more scaly than usual. Before coming under my care a diagnosis of syphilis had been made and antisyphilitic remedies had been employed for some months, of course without influencing the disease. Under the local use of a 2 to 3 per cent. alcoholic solution of salicylic acid and the internal administration of quinin in considerable doses, there was a steady but slow improvement in all the patches; on the back and arms the improvement was especially noticeable, the disease disappearing in these regions in the course of a few months. Other local remedies were tried from time to time, but the salicylic acid seemed by far the most effective. After nearly a year of this treatment, improvement ceased and as there had been no new patches, trichloracetic acid was applied to the thicker lesions at intervals of some weeks, the intervals between the applications being longer than was desirable because of the distance at which the patient lived from Philadelphia. These applications were of undoubted value, but as the patient found them extremely painful they were discontinued and phenol every few days substituted, the patient making the applications herself. Two months later a decided improvement was noted, and the treatment was continued. In the latter part of January of this year a most extraordinary change was observed in the disease—all of the patches were apparently undergoing rapid involution and some of the smaller and less pronounced ones had almost entirely disappeared. It was then learned that this remarkable improvement had followed immediately on the extraction of a "capped" tooth which a roentgen-ray examination had shown to have an abscess at the root, although it had not given the patient any trouble for years. On extraction the roots of the tooth were found to be badly necrosed. Unfortunately, under the circumstances, a bacteriologic examination of the abscess was impossible; this is greatly to be regretted since it leaves us in entire ignorance of the character of the organism concerned in the infection. I had hoped to see this patient again before the completion of this paper, but circumstances have made that impossible. In a recent, letter, however, she states that there has been further improvement.

This case is reported simply for what it is worth—not as proving or disproving anything as to the etiologic relationship of focal infec-

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

tion to erythematous lupus, but to put on record a case which is, to say the least, suggestive to a considerable degree of the possibility of such a relationship.

OTHER CASES

A few years ago, Barber[1] reported an extensive case of acute erythematous lupus following the ordinary chronic type after some years, accompanied by high temperature and other grave symptoms threatening, for a time, the patient's life, in which a bacteriologic examination of the feces revealed the presence of large numbers of *Streptococcus longus,* the organism growing in almost pure culture on inoculated mediums. After an illness lasting for a month or more, the patient recovered, the eruption vanishing rapidly. With the improvement in the eruption the streptococcus disappeared from the feces. In Barber's opinion, the disease was due in this instance to the absorption of a toxin produced by the streptococci found in such abundance in the intestinal canal. No mention was made of any local focus of infection and apparently no search was made for it beyond the examination of the feces. Recently[2] the same author has reported two cases of erythematous lupus of the ordinary type associated with an infection of the tonsils by the same organism found in the former acute case; and from a series of similar cases which he has been able to collect recently he is convinced that the disease is due "in some instances at any rate" to the toxins produced by *Streptococcus longus.* In one of the reported cases treated by an autogenous vaccine prepared from the tonsils, an injection of a dose containing 5,000,000 of the organism was followed by a decided reaction in the patches of lupus lasting twenty-four hours; and after a larger dose, one containing 10,000,000, an intense reaction followed, together with considerable constitutional disturbance. The streptococcus in this case was found not only in the tonsils, but also in adenoid tissue at the back of the throat, the patient having suffered from adenoids some years before. It should be added that uniformly positive results followed a series of tuberculin tests made according to the method of von Pirquet.

Although negative evidence is of comparatively little value as compared with positive findings, I cannot refrain from referring briefly to a second case of this affection which has been under my close observation for a period of four years. The patient is a robust man apparently in excellent health, apart from his cutaneous disease, about 50 years old, and his disease has lasted seven or eight years. It occupies and is limited to both cheeks. The eruption is quite florid in appearance with a moderate amount of infiltration, especially about the borders. A recent roentgen-ray examination by one of the most skilful roentgenologists in the country and a thorough inspection by a competent dentist have failed completely to disclose any disease of the teeth. A thorough examination of the throat and especially of the tonsils has disclosed nothing abnormal; the tonsils are quite small and are completely hidden between the pillars of the fauces. The patient is positive in his statements that he has never had any trouble with his throat. In conclusion, it may be stated with confidence that there is no disease of either teeth or tonsils, and that there have never been any symptoms suggesting the presence of focal infection elsewhere.

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[1] Barber: Brit. J. Dermat. **27**:365, 1915.

[2] Barber: Brit. J. Dermat. **31**:186 (Oct.-Dec.) 1919.

Truly, "experience is fallacious and judgment difficult."

DISCUSSION

Dr. Pusey recently had a case analogous to Dr. Hartzell's which suggested the possibility, as Dr. Hartzell's had, of the causal relationships of focal infection to some cases of erythematous lupus. This case was that of a young woman with severe erythematous lupus of long standing on the face, the patches showing a good deal of infiltration and thickening; they were elevated and of a dark chronic red color. This woman's teeth had been found to be in bad condition, most of them showing alveolar abscesses, for which removal had been advised. On the removal of the teeth there was a temporary exacerbation, but in the course of a month there was distinct improvement. Two months later the improvement continued. He was glad that Dr. Hartzell had called attention to this possible factor in erythematous lupus, but, like Dr. Hartzell, he thought that focal infections were only one of the many sources of intoxication that might produce erythematous lupus.

Dr. Schamberg wished informally to place on record another case of acute fulminating erythematous lupus. The patient was a woman, about 40 years of age, with an ordinary lupus erythematosus on the face, who developed an erysipelatoid appearance of the facial lesions, new patches on the body, and in whom a pneumonic consolidation with high fever caused death in a few days. Unfortunately, he was unable to obtain a necropsy examination.

In regard to the work of Barbour, which had been quoted, we should certainly be extremely reserved about accepting any direct relationship between the streptococcus and lupus per se. He did not think anyone had succeeded in establishing fixed types of streptococci which had specific pathogenic effects. Some years ago he made cultures of the throats of 100 patients with scarlet fever and these were bacteriologically studied by Dr. Gildersleeve, who found 92 per cent. of streptococcus in these throats. Cultures were then made from 100 apparently healthy university students in whom 82 per cent. showed the streptococcus, and these killed guinea-pigs with as much rapidity as those from the throats of the scarlet fever patients. Furthermore, the streptococcus was present in the throats of most persons.

In regard to the improvement which occurred in one of the reported cases of lupus erythematosus from vaccines, it was possible that this was the effect of a nonspecific protein. It was well known to dentists that exacerbation of symptoms for which the patient sought relief often temporarily followed the extraction of incriminated teeth. This is believed to be due to absorption of organisms from the vascularized infected focus. It is conceivable that an absorption of nonspecific organisms might also bring about improvement.

Dr. Wallhauser reported a case which terminated fatally. The patient was a woman who had developed an eruption over the bridge of the nose which extended out over the cheeks; this had persisted for about one year—the color was a deep purplish red with superficial scaling. The resemblance to lupus erythematosus was striking, but some of the characteristic features of this condition were lacking—elevated border, atrophy, etc. Febrile symptoms were present, the temperature ranging from 99 to 104 degrees. A focal infection was carefully considered and every effort made to locate the source, with a negative result. The patient gradually passed into a state of coma and died; the postmortem examination revealed an abscess of the liver.

Dr. Fordyce agreed with Dr. Pusey that lupus erythematosus might have a multiform etiology. He was convinced that a certain percentage of cases were related to tuberculous foci somewhere in the body. He had reported, at a former meeting of this association, a case of lupus erythematosus of the face in which a tuberculous focus was found in the kidney at necropsy. He had seen numerous cases of lupus erythematosus with coincident tuberculous lymph nodes in the neck. In one of these cases, after an operation on the lymph nodes, numerous patches of lupus erythematosus appeared on the face. Years ago Dr. Fordye reported symmetrical patches of lupus erythematosus on the hands and forearms of a pregnant woman who developed convulsions before her confinement. The lupus erythematosus disappeared after her confinement.

Dr. McEwen said that as the subject of focal infection was almost certain to occupy increasingly the attention of dermatologists, he wished to mention two points. First: Is one warranted in saying that the tonsils are not foci by simply saying that they do not appear to be, because they are buried and small? He knew of a case in which there were pronounced joint symptoms; when the small, fibrous, and deeply buried tonsils were taken out they were found to contain visible pus. Second: In looking for foci the gall tract should not be forgotten. The gallbladder and ducts are often the seat of a chronic infection which may become focal in effect, but the profession is so prone to think of the teeth and tonsils as the only foci that this fact is apt to be overlooked.

Dr. Corlett stated that he had always been of the opinion that lupus erythematosus was not associated clinically with tuberculosis or lupus vulgaris. He never yet had seen a case of lupus erythematosus associated indubitably, other than by family history, with lupus vulgaris or tuberculosis. About a year ago, however, when Dr. Stokes presented his valuable study relative to foci of tuberculosis giving rise to or associated with lupus erythematosus, he realized that many cases might harbor foci of tuberculosis that were not demonstrable by ordinary examination or apparent from visual inspection. That lupus erythematosus was caused by other agencies and that reflex nerve irritation might be a potent factor in its causation Dr. Corlett had also believed. The latter belief was borne out by certain observations; one he especially recalled, made a number of years ago, in a woman who was a stenographer, whose eyes had been corrected by some traveling optician and who had a very extensive lupus erythematosus, not of the ordinary butterfly form, but surrounding the palpebral region. A careful examination of the eyes by a skilled oculist and proper glasses brought relief in the course of some months, so that the ordinary applications that had been useless before were effective in producing a cure.

Again, as a possible cause of lupus erythematosus, foci of infection may be encountered in the teeth, as evidenced by two cases of herpes in a woman whose teeth were in a very bad condition and whose mouth was a source of irritation, reported last year before this Association. After the teeth were put in proper condition or extracted, no attack of the skin manifestation took place and finally, after some months, the cutaneous symptoms all disappeared.

Since that time Dr. Corlett had had a case of inflammation of the cheek which resembled a circular patch of eczema and which was very obstinate to treatment. Various applications had no effect. This woman received numerous roentgen-ray examinations, and well defined abscesses were found. These were removed and the mouth properly treated. In the course of a few weeks the lesion on the cheek began to heal and in due course finally disappeared.

Dr. Corlett wished, however, to give a word of warning against extracting teeth indiscriminately. The average practitioner, reading a report of this sort, was apt to think that everything dermatologic was due to infected teeth, and during the last few years there had been more sound teeth extracted than one would think possible. He felt that the profession should be on guard against attributing indiscriminately various infections to the teeth, although they must also recognize that such an infection was often effective in producing various disorders.

Dr. Highman thought the question raised by Dr. Hartzell's presentation was of tremendous importance in relation to such a clear cut condition as lupus erythematosus. It should be borne in mind that one was dealing with a distinct clinical entity. When the question of etiology came into consideration, one was at once confronted with the fact that here again was an example, in a very restricted manner, in which tissue was able to respond uniformly to various pathogenic causes. He had seen one case which in one way was a parellel with Dr. Hartzell's and in the other was like the cases brought out by Jadassohn. The case was that of a woman of about 20 years of age who for six or eight months had had malaise and weakness. She developed a patch of lupus erythematosus and complained of a peculiar, bandlike headache. Dr. Highman sent her to an otolaryngologist, who found an empyema of the antrum of Highmore. Under treatment of the latter, the lupus erythematosus began to disappear. Whether this was an example of focal infection in lupus erythematosus, he did not know. He was not a focal infection "fan," for every nook and cranny of the body might contain a bit of pus and he did not believe that every disease such a patient had must arise from that focus. Nevertheless, it did seem that when a condition of this sort was present, and when after the removal of the focus it disappeared, that there must be some relation.

Dr. Highman had seen some cases connected with tuberculosis. The whole literature was full of such cases (Jadassohn). Kyrle reported lupus erythematosus on one cheek and lupus vulgaris on the other. Everyone had seen lupus erythematosus associated with papulonecrotic tuberculids, and even some lesions in the Darier-Roussy type of sarcoid had distinctly the clinical appearance of lupus erythematosus. There was no getting around these facts. Thus there seemed to be some connection between lupus erythematosus and tuberculosis.

Dr. Stokes had seen within a comparatively short time two cases with extensive erythematous lupus of the face which had completely recovered for the time being following erysipelas. The patient had apparently experienced a kind of fortuitous vaccine therapy. One should be particularly careful not to allow such observations to lead him into unwarranted conclusions as to streptococcal etiology.

With reference to an association with tuberculosis, he had seen many striking instances of it. His study of the association of streptococcal foci with tuberculids had led him to offer the hypothetical suggestion that cutaneous sensitization from a pyogenic focus might serve as a secondary etiologic factor in the production of erythematous lupus with tuberculosis as a primary etiology or the reverse. In this way erythematous lupus might be regarded as a toxic or allergic manifestation of associated tuberculous and streptococcal focal infections.

Dr. Hartzell (closing) emphasized the fact that while it was not common, erythematous lupus occasionally disappeared spontaneously, a fact which made it difficult to decide as to the action of any particular remedy. He had seen two cases of that sort. If he had given the impression that he was arguing for an etiologic relationship between erythematous lupus and focal infection, he had given the wrong impression. It was not his purpose to argue either for or against such a relationship; he simply wished to report a case which impressed him very much on account of the improvement following the removal of the teeth.

As to the multiform etiology of erythematous lupus, that might be true, but he disliked very much that sort of conclusion about disease—it seemed to him a sort of compromise. It was true that a number of diseases have a multiple origin, but before deciding anything in that respect, one should be quite sure of it.

XV. TREATMENT OF GENERALIZED PSORIASIS *

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ST. LOUIS

When the idea to present a paper on the treatment of this disease came to mind the subject seemed simple enough, but a consultation with the literature soon convinced me that a textbook on the subject was more in order than a paper, so the title more properly should have read: "A Note on Another Method of Treating Generalized Psoriasis."

Intelligent people suffering from the disease learn within a comparatively short time to carry their handicap with little trouble, but its presence is always a handicap, ever demanding more or less embarrassing explanations on its discovery by another person. This was especially true in army life.

Apology may be made for the severity of the course to be outlined, but since the necessity in war developed the method it may prove of future value until the specific or a more rapid method is discovered. The etiology being unknown a specific for its eradication, temporary or permanent, is wanting. It would of course be folly to suggest any line of treatment that would produce favorable results in all cases or varieties, for we well know the resistance to all forms of treatment of the parasoriasis group, as well as individual cases of the ordinary typical psoriasis.

It is not my intention to discuss the various remedies, drugs, diets, or electrically generated methods—they all have their place and are valuable—but to present to you a new combination with an old, and in our opinion, the best drug for the removal of the lesions in generalized cases, namely, chrysarobin. Most patients with a few, or frequently with many lesions, are more or less indifferent to their presence, but when the lesions become generalized and unsightly and manifest subjective symptoms a radical course of treatment is necessary.

In 1904 the author learned the treatment of generalized cases with the Dreuw ointment and up to a short time ago we have relied on it, but in 1918, while with the American army in France, two weeks were spent in the largest British skin hospital at Hardelot, France, observing their methods of treating diseases in soldiers. There were four expert

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* Studies, reports and observations from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., Service of Drs. M. F. Engman and W. H. Mook.

* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

dermatologists under Lieut.-Col. Henry MacCormac of London, treating from 1,500 to 2,000 skin patients most of the time. During my stay of two weeks in February there were about eighty patients with psoriasis, most of them with profuse lesions. It is to Dr. H. W. Barber of London, a member of the staff at that time, that I am indebted for the formula presented in this paper. Since saving of man power was absolutely necessary, time was the most essential factor in treatment. Barber informed me that he had experimented with many drugs and had finally evolved a formula of 2 per cent. phenol and 10 per cent. chrysarobin in petrolatum as the best combination. He had read somewhere that phenol enhanced the action of certain drugs and on trial with chrysarobin he was able to reduce the hospital stay of soldiers suffering from psoriasis. Since my return last June we have had such marked success in cutting down the duration of treatment that it is thought advisable to publish our method in detail.

The patient is informed that he must go to a hospital or be confined to his home under the care of a nurse for a period of from twenty to twenty-five days. He must be visited daily. Owing to the danger of chrysarobin dermatitis, as well as destructive action of chrysarobin on clothing and bed clothes, confinement to a room or hospitalization is necessary. Three ointments are used, the amounts of the drugs to be varied to suit individual reactions and idiosyncrasies.

TREATMENT OF SCALP, FACE AND HANDS

Salicylic acid and white precipitate of mercury, 5 per cent. each, in white petrolatum, is to be rubbed into the scalp once daily. The percentage of the drugs may be increased cautiously. If lesions exist on the hands or face half these strengths may be used. Tar ointments may be used in patients with an idiosyncrasy to mercury.

TREATMENT OF THE BODY

Two ointments are necessary—one to prevent as much as possible and to relieve, the chrysarobin dermatitis. First a soothing application is used: 1 per cent. ichthyol (or a substitute), corn starch and zinc oxid, 6 per cent. each, in white petrolatum. This is to be applied to the normal skin between patches before the chrysarobin ointment is applied. It is also to be used after the chrysarobin dermatitis has developed. Second, a chrysarobin ointment, which consists of 2 per cent. phenol and 10 per cent. chrysarobin in white petrolatum, is applied. These amounts will be advantageous in a majority of cases, but may be decreased or increased when advisable. The patient should be warned of the danger of conjunctivitis from chrysarobin and instructions given to prevent its occurrence.

After the ichthyol or soothing ointment has been applied to the normal skin between the lesions, preferably with a wooden tongue depressor or spatula, the chrysarobin ointment is applied to the lesions with a swab made of cotton or gauze twisted on the end of a stick. Stiff brushes are to be avoided as too irritating. Corn starch or talcum powder is then dusted plentifully over the entire body and the patient advised to abstain from walking or exercising as much as possible, though it is not necessary to remain in bed. Bandaging the extremities is not necessary and causes discomfort. A large arm chair in the room will add to comfort.

Applications are made once daily until the chrysarobin dermatitis begins to develop, and it is at this point that the greatest skill in the treatment must be manifested. The chrysarobin must be discontinued if severe reaction develops. An occasional corn starch and soda bath may be advisable as a rest and for cleansing purposes, using two cups of starch and one cup of baking soda to the bath tub full of warm (not hot) water.

The skin will be discolored after the first treatment and after three to six days the skin generally becomes much reddened, but with less real inflammation than is usual when chrysarobin alone is used. The ointment is not to be discontinued unless the distress from burning and pruritus is unbearable. If the chrysarobin must be discontinued for a few days, the soothing salve is applied twice daily until it may be resumed. In some patients the chrysarobin may be applied continuously until all lesions have disappeared. In a few, two applications daily are possible, but in a majoirty rest is indicated after five or six days. Occasionally persons with idiosyncrasy will be encountered and in these the method is useless.

SKILL NECESSARY IN USING THIS METHOD

The objections to the method are many and individual skill must be developed. Certainly it is a dangerous weapon for the unskilled. The confinement to a room or hospital, the destruction of a certain amount of clothing and the physical discomforts that may be encountered are obvious, but when necessity or desire demands a rapid removal of lesions with a favorable assurance of success, we can heartily recommend it.

DISCUSSION

Dr. Schamberg said that the action of chrysarobin on the skin appeared to depend on three factors: First, its powerful reducing effect; second, its marked affinity for the keratin or epithelial tissues, and, third, its relative stability or the slowness with which it undergoes oxidation. The stain cannot be removed from the epithelial cells by boiling with strong acids or alkalies. When it becomes oxidized it develops into chrysophanic acid, which is therapeutically relatively inert.

Every one realizes that drugs like chrysarobin have a great influence on the lesions of psoriasis. It is a common observation that in the acute developmental stage of the eruption drugs like chrysarobin often cause a spreading or extension of the eruption. He believed there were three stages of the disease, the developmental, the quiescent and the stage of spontaneous decline. If the disease was attacked in the active developmental stage with arsenic internally or chryasorabin externally, harm was commonly done, but these drugs during the quiescent stage had a marvelous effect on the eruption. Was there any way of converting the developmental stage into the stage of quiescence? Dr. Schamberg thought two procedures were of value for this purpose: first, the use of a low protein diet and, second, the administration of autoserum injections. He had recently had two most rebellious cases of psoriasis in which no active remedies could be used without doing harm, but after the use of several autoserum injections the active stage of the disease was rendered quiescent and the drugs that could not be tolerated before could be tolerated and were highly efficient in bringing about an almost complete disappearance of the eruption.

Dr. Engman asked what was the peculiar action of the psoriasis itself between the white halo and the surrounding skin which became pigmented.

Dr. Schamberg, replying to Dr. Engman, said he did not think the reason for this was known. Every one had observed, he was sure, in psoriasis patches treated with chrysarobin a small halo, perhaps a quarter of an inch in width, around the psoriasis patch, which failed to take the stain, owing to some peculiar feature of this border area and the lack of affinity between the keratin at this margin and the chrysarobin.

Dr. Grindon stated that the white halo around the patches had long interested him. He had long thought that the explanation just given by Dr. Schamberg was the correct one, but he had changed his mind, when he observed the same white halo around the patch when dermatitis was excited by the Kromayer lamp as when chrysarobin was used. The cause evidently lay in the skin itself and not in the agent employed.

As to the use of chrysarobin, Dr. Schamberg was right in saying that it was harmful when used in the active stage of the attack. Dr. Grindon believed that we often made a mistake in using chrysarobin in too great strength. He was at one time fond of using the Dreuw ointment. There was no doubt but that chrysarobin would clear up many cases, but new lesions were sometimes provoked by the dermatitis. He did not now use it stronger than 2 per cent. and in most cases obtained as good an effect as from the stronger ointment. There was a simple method which gave as good results as any other in chronic and refractory cases. Patients take two baths a day, at a comfortable temperature, remaining in the bath perhaps an hour each time, with half a pound of sodium bicarbonate in the bath. Results were not striking, but neither were they by other methods, and this was as good as any.

Dr. Irvine thought that whatever the etiology of psoriasis, we must recognize that many factors serve to aggravate it and bring on attacks. In a generalized psoriasis more could be done by directing the conduct of patients along the lines of general hygiene than by the particular use of any one drug. His patients had shown more improvement from this than from any other method. The improvement of bad hygiene and improper diet had a good effect. Dr. Irvine thought it was also well to emphasize the hospitalization. Much more could be done for generalized psoriasis by putting the patients to bed where their habits could be controlled than by using any combinations of or single drugs in treating the skin. In his opinion, this was of such great importance that he tried to use those drugs that were the most satisfactory to the patient, namely, those easiest and pleasantest to use. He found in his patients that with the use of a daily bath and a simple ointment, such as salicylic acid and sulphur, and putting them to bed they got along just as well as with something disagreeable like chrysarobin, the dirty tars or other things of a like nature.

Dr. Highman said that the discussion of the treatment of psoriasis always stimulated oratory and every one had a series of experiences that never seemed to jibe with those of his colleagues. In rendering the lesions quiescent in the sense brought out by Dr. Schamberg, Dr. Highman did not understand the relationship of diet to the matter, or that of autoserum. His own experience, so far as low protein diet was concerned, could be illustrated by examples. One case was that of a woman of 40 or 45 with generalized psoriasis extending from the ankles to the shoulders. She had been on a rice diet for six months and had become despondent, largely through starvation. When she was put on a bland mixed diet the lesions on her body began to involute rapidly. The local therapy was 2 per cent. salicylated petrolatum. He had never seen that formula accomplish anything in psoriasis before, but he had to use something to keep the skin pliable because it was practically lichenified all over the body. The same thing was illustrated in a clinic in New York. A young woman came in and the doctor said, "I want you to stop eating meat and eggs," to which the patient replied, "I have never in my life eaten either." These things were difficult to reconcile.

Dr. Howard Fox was much interested to hear Dr. Schamberg's reference to autogenous serum injections. He had had no further experience with this procedure for the past few years. In regard to the chrysarobin treatment of psoriasis, he wished to call attention to the value of impermeable dressings to cover the chrysarobin applications. This plan was generally known but seldom followed. In some obstinate cases he felt that the action of the chrysarobin was greatly increased by covering the skin with oiled silk or rubber cloth, which prevented the evaporation of sweat and caused maceration and softening of the scales. It was on this principle that entire suits of similar materials had been previously employed by some of the dermatologists of Vienna.

Dr. Towle was of the opinion that the intensity of the symptoms could be much mitigated by diet. Last year they carried out a number of series of experiments which corroborated it in every detail. In addition to that, as was mentioned by Dr. Grindon, prolonged hot baths, sometimes prolonged, one, two or three hours, were given and under these conditions chrysarobin was found to be more effective. The heat unquestionably had something to do with it. Another method of mitigating the intensity of the eruption in patches that were not too large was the application of crude coal tar, which would dry lik gutta percha. Some quite remarkable results had been achieved with that method. The cutting down of the diet seemed to enhance the action of the drugs. There was an old-fashioned remedy—the internal administration of potassium acetate—formerly used in connection with chrysarobin. This was sometimes useful.

Dr. Hartzell asked Dr. Mook whether he ever observed any evidence of phenol poisoning. In his opinion the application of a 2 per cent. ointment was not free from danger. He cited a case of universal psoriasis seen a year or two ago in which, according to the patient's statement, a daily dose of 10 grains of sodium cacodylate had been given hypodermically for an entire year with no untoward result; during this time the eruption had almost completely disappeared.

Dr. Haase recalled the fact that he spoke several years ago of the use of crude coal tar, straight from the gas house, in treating psoriasis. He had obtained good results from that treatment. In one case he applied it to a generalized psoriasis and the lesions cleared up, but in a short time the man had an albuminuria and he feared that was due to the application of tar all over his body. So he was now limiting the use of straight-run crude coal tar to localized patches of persistent psoriasis.

He had recently had an interesting experience in a young boy with reference to the use of phenol. The boy had a persistent, ugly patch on each knee. On one knee he had a rather deep-seated furuncle. The surgeon used a 2 per cent. phenol ointment on the furuncle and the patch of psoriasis. With the disappearance of the furuncle the psoriasis disappeared. When tried on the other knee it had no effect.

Dr. Wile thought there was no doubt that Dr. Mook saw the marked improvement under the method described, but a point had occurred to Dr. Butler and himself—had not the rapid improvement been due largely to the fact that he hospitalized the patients? Most of the patients were ambulatory and in many instances when they were persuaded to come into the hospital for treatment, the mere fact that they remained in bed and devoted the greater part of their time to the treatment greatly shortened an attack. He wished to know whether Dr. Mook did not agree to this.

Dr. Wise believed Dr. Mook's paper referred chiefly to soldiers treated in the army and the discussion was more directed toward treatment of psoriasis in general. He knew that Dr. Mook had used Dreuw's ointment.

Another question he wished to ask was whether the addition of salicylic acid would increase the efficiency of the new formula?

One thing that had not been mentioned was the roentgen ray. Dr. Mook had stated that it took twenty-five days to clear up the average eruption, which was the average time for any psoriasis without the application of an ointment, and without the inconvenience and staining associated with the use of chrysarobin.

Dr. Hazen recalled two cases of generalized psoriasis that lasted all winter in spite of most of the treatments mentioned and when the bright, sunny days of spring came both patients became well within two weeks.

Dr. Smith was interested to know whether others had noted this condition. A young woman who had had a mild psoriasis for several years showed an acute exacerbation at the height of which she developed an acute attack of tonsillitis, and the psoriasis practically disappeared. The complete resolution of the lesions was rapid and as far as he knew there had been no recurrence. This might be simply a coincidence.

Dr. Stokes thought hospitalization was a prominent factor in the improvement of patients, largely because they devoted nearly all their time to treatment. He had found that if he could induce a psoriatic patient to spend even a week in the hospital he could greatly increase the efficacy of treatment.

Dr. Fordyce thought it more important to have a committee appointed to standardize the treatment of psoriasis than of syphilis. He had one or two suggestions to offer. One was the use of a 30 to 50 per cent. ammoniated mercury ointment in psoriasis of the scalp and face. The lesions yielded more rapidly to an ointment of this strength than to the one usually employed. Occasionally mercurial stomatitis followed its use. He said that better results would be obtained if chrysarobin ointments were applied by a trained nurse or by some one familiar with their use. When the applications were entrusted to the patient alone, they were not as a rule used in a manner to bring about the best results. It was important in treating patches of chronic psoriasis to produce a decided reaction in and about the lesions. It was furthermore important in his opinion to cure all of the lesions, as by so doing relapses would probably be less frequent.

Dr. Varney expressed the opinion that the paper had offered some valuable suggestions, and in speaking only of generalized psoriasis, which all had trouble in relieving, he emphasized the sunlight treatment that Dr. Hazen had just mentioned. At this time of the year we can get a welcome relief for rebellious psoriasis patients by prescribing sunlight in a definite way. He was more likely to tell a patient to get into B.V.D.'s and a canoe and spend a given length of time, increasing this each day, in the sunlight on the water between 11 and 2 in the day time, as he was to prescribe any local drug treatment. He believed this would do more toward clearing up a large percentage of generalized psoriasis than any other form of local treatment. From the last two weeks in May until the middle of September, we have the most direct chemical sun rays, if they can come through clear air instead of the smoke screen that hangs over our cities.

Dr. Engman said he had observed the treatment that Dr. Mook had learned in France, and he thought it the most rapid treatment he had yet seen. One little therapeutic sign that he had found of value was brought out by Dr. Schamberg, who spoke of the difference in the degrees of the different stages of psoriasis. They found that in acute attacks and in chronic persistent attacks a systemic shakeup was a good thing. Some years ago, in experimenting with foreign proteins in various diseases, they found that psoriasis could be eradicated by bringing up a high temperature by doses of foreign proteins. Just why this was the case he did not know. They had been using typhoid vaccine and by injecting a dose every four days the psoriasis would usually begin to disappear quite rapidly. A change occurred and then by applying chrysarobin or some other drug and giving the patient a hot bath it seemed to increase the effect of the drug. Dr. Engman had never seen this method cause an attack of psoriasis to disappear, but he had seen it assist materially in other forms of treatment.

Dr. Mook (closing) said that early in his dermatological career he had a sad experience with psoriasis. While in the Skin and Cancer Hospital in New York a young man came in with a generalized distribution of this disorder and he had just learned about the treatment with Dreuw's ointment. The scales in this case were so thick that he conceived the idea that a good way of getting rid of them in a hurry would be to put on green soap for about half an hour. This was done and he then advised the application of Dreuw's ointment all over the body. In half an hour the patient was unconscious and the only symptoms to guide him were profuse perspiration and rapid pulse. He finally made a diagnosis of salicylic acid poisoning. The symptoms of severe poisoning persisted for thirty-six hours, but the man finally recovered.

In regard to the treatment of generalized psoriasis, every one knows about using chrysarobin only in the quiescent stage. In the British army, with eighty or 100 cases all the time, they showed that most patients could be treated with chrysarobin even in the developmental stage. Barber had been experimenting with psoriasis for three or four years. It was troublesome and with somewhere around 100 men in the hospital all the time from this disease it was serious in loss of man power to the British army. Since his return to private practice he had been putting practically all his patients on this ointment. Years ago he used the unequaled Dreuw ointment in practically all cases. He believed, in treating a large number of patients with large lesions, the stronger ointment was necessary to produce a dermatitis and chrysarobin reaction. If it can be controlled just short of the intense burning and itching the lesions disappear more rapidly than without the reaction.

The point brought up by Dr. Engman was a very striking one at that time and they saw lesions of generalized psoriasis almost disappear in seven or eight days, but if the patient was left alone inside of two or three weeks they would reappear. In the treatment of generalized cases, they found that it was better to remove every single lesion on the body and Dr. Mook thought this was important, especially about the scalp, elbows and knees. The chances for early recurrence were thus much lessened.

He used radiotherapy in a few selected cases. One of the first things they do at the Barnard Skin and Cancer Hospital is to teach the patient as much as possible about this disease. He had taught many patients to use Dreuw's ointment and most of them knew the treatment and their individual reaction as well as Dr. Mook did, and carried out the treatment themselves.

Dr. Wise had asked about the comparison of the new treatment with the Dreuw ointment. Dr. Mook had four patients whom he tried out, formerly treated with Dreuw's ointment. Some patients come once a year or every two or three years. When they developed a profuse eruption they would come in and stay in the hospital until they were well. The average time for acute cases of psoriasis under the Dreuw ointment treatment was from five to six weeks. With the new treatment this had been reduced in one case to nineteen days, in one to twenty-one days, and in one to twenty-four days, so the matter of a reduction of two weeks in the treatment was quite important for army purposes. The treatment was dirty and it was difficult to put patients in the hospital, but if they went they recovered from their psoriasis.

In regard to hospitalizing and rest in bed, there was no doubt but that rest would change the condition of the psoriasis as well as in many other skin affections. So far as attempting to remove psoriasis in a short time was concerned, the rest would not do it.

In regard to phenol poisoning, Dr. Barber said he had treated many cases and watched the urine carefully, but he had never seen any phenol poisoning or albumin in the urine following the use of this treatment.

Radiotherapy may be used over certain areas of the body, but it is rather a dangerous procedure unless one is well trained in the use of the Coolidge tube, with massive doses, and he thought it would be dangerous in cases of psoriasis to repeat this treatment every three or four years in succession.

This treatment only referred to those who had severe symptoms and wanted to get rid of the eruption in a short time.

A MENACE IN THE LOW PROTEIN DIET *

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Since the investigation of Schamberg[1] and his collaborators on protein metabolism in psoriasis and the distinctly beneficial results obtained by them in this disease by restricting the nitrogenous intake, it has become more or less a routine with a great many dermatologists to place patients with psoriasis on a low protein diet. The use of such a diet has not been confined to psoriasis; it is being advised in a number of other dermatoses—dermatitis, to instance one.

In reducing the protein intake, the caloric requirements are made up usually by that of carbohydrates and fats. Practically, the increase occurs most often in the carbohydrate components, since they are more agreeable to the majority of patients. A diet of this kind, rich in starches and sugars and poor in proteins, may be kept up for a long time, either by order of the physician or by the patient's own volition.

It is not my intention to discuss the value or uselessness of this diet; but owing to its widespread adoption, it becomes of importance to call attention to a possible danger, and thus, to a contraindication to its use, in certain patients.

Diabetes is recognized universally as a contraindication to a diet rich in carbohydrates; but it is not so generally realized that there exists a detectable prediabetic state in which a diet of this type sooner or later leads to permanent glycosuria. To continue a prediabetic patient on a diet composed of large amounts of carbohydrates is tantamount to condemning that person to diabetes. Two cases recently under observation exemplify these points.

REPORT OF CASES

CASE 1.—Miss B., aged 22, first seen May 6, 1920, had psoriasis which began six years ago. In June, 1917, she had an acute, generalized attack. At this time she was treated with fractional doses of roentgen ray and placed on a restricted protein diet. The eruption wholly disappeared, but recurred in April, 1920, a few patches presenting on the scalp, elbows and thorax. For two and one-half years she remained on the diet first prescribed, because she was told that it might prevent recurrence. Her diet consisted mainly of potatoes and bread, smaller quantities of coarse vegetables and a small piece of meat every other day.

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* From the Department of Dermatology and Syphilology, College of Physicians and Surgeons, Columbia University, New York.

[1] Schamberg, J. H.; Ringer, A. I.; Raiziss, G. W., and Kolmer, J. A.: Summary of Research Studies in Psoriasis, J. A. M. A. **63**:729 (Aug. 29) 1914.

She was overweight and flabby, with a pale, pasty complexion and puffiness about the eyes that suggested a diabetic habitus. There was complaint of polydipsia, polyuria and nocturia. A general physical examination was negative except for a persistent pulse rate of 100.

June 17, 1920: Urinalysis showed no sugar.

June 24, 1920: A glucose tolerance test gave the following result: blood sugar (before glucose), 0.142 per cent.; urine sugar, negative.

10 a. m.: Glucose, 100 gm., in 200 c.c. water.

	Percentage of Blood Sugar	Urine Sugar
10:30 a. m.	0.344	Positive
11:00 a. m.	0.300	Positive
12:00 m.	0.248	Negative
1:00 p. m.	0.178	Negative
2:00 p. m.	0.162	Negative

Marked nausea continued for twenty-four hours.

This test showed a prediabetic state of advanced grade. The appearance of glycosuria was particularly ominous and definitely pathologic. It was evident that a diet rich in carbohydrates was strictly contraindicated. The diet, therefore, was changed to conform to the findings, and the psoriasis treated with roentgen ray, under which it has cleared up except on the scalp.

July 8: Blood sugar, 0.140 per cent.; urine sugar, negative. She was still hyperglycemic, which if persistent, indicates the need of fast days.

This case exemplifies three important facts: (1) the inadvisability of instituting a diet rich in carbohydrates without previous knowledge of the patient's ability to take care of it; (2) that absence of glycosuria is not always an index of safety; and (3) that a glucose tolerance test may indicate a state of grave danger to the patient, which may be aggravated unwittingly by a rich carbohydrate diet, such as is usually instituted when psoriatic patients are placed on low protein intakes.

Case 2.—Mr. E., aged 24, first seen June 8, 1920, had a widespread seborrheic dermatitis which had been present for many years. At present it was severe on the scalp, face, arms and thighs. There have been occasional remissions but never complete freedom. He had been treated by various means for years without avail. Two years ago he was placed on a low protein diet and had voluntarily continued it since. He subsisted principally on coarse vegetables and starchy foods. During the first year of this diet, he took no animal food; for the past twelve months he had eaten an occasional piece of beef or chicken.

In an endeavor to discover an etiologic factor, a glucose tolerance test was performed. The results were: blood sugar (before glucose), 0.093 per cent.; urine sugar, negative.

10:15 a. m.: Glucose, 100 gm., in 200 c.c. water.

	Percentage of Blood Sugar	Urine Sugar
10:45 a. m.	0.264	Negative
11:15 a. m.	0.188	Negative
12:15 p. m.	0.176	Negative
1:15 p. m.	0.166	Negative
2:15 p. m.	0.162	Negative

He had no nausea.

Lowered glucose tolerance is well demonstrated in this test. Glycosuria did not occur, but the failure of the blood sugar to return to a normal figure inside of four hours is significant of lowered sugar assimilability. It can be assumed that this patient would be injured by a persistently high carbohydrate intake; perhaps eventually to a stage of pancreatic hypofunction leading to permanent glycosuria. Certainly the diet that had been advised for the seborrheic dermatitis was contraindicated in view of the potential diabetes elicited by the glucose tolerance test. He was, therefore, placed on a diet conforming to this finding.

REMARKS

The important point is the detection of the potential diabetes; when that has been ascertained the physician becomes master of the situation. Should he elect to continue a low protein diet, it is possible, in most cases, to achieve his purpose, and still maintain a carbohydrate and protein intake consonant with the conditions confronting him. By frequent blood sugar estimations, a record can be obtained, which will determine whether the campaign is to be maintained or abandoned. Prediabetic patients should be told of their condition, its control and dangers, so that they do not unknowingly adopt a diet which is fraught with danger to them.

The question whether a rich carbohydrate diet can, of itself, cause diabetes is still sub judice. Experimental evidence apparently shows that this disease can be produced only when a latent tendency toward it already exists. No amount of sugar feeding to normal animals causes diabetes in them; but animals which by operative procedures have been rendered latent diabetics, may develop the condition by overfeeding with saccharin substances. Allen [2] believes that the increase of diabetes in civilized peoples is due to the stirring up of a latent tendency by a combination in which mental stress and rich carbohydrate diet are the principal elements.

CONCLUSIONS

1. Most patients, on a low protein diet, receive an increased carbohydrate ration.

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[2] Allen, F. M.: Glycosuria and Diabetes, Cambridge, Harvard University Press, 1913, pp. 592 and 1062.

2. A diet rich in carbohydrates is contraindicated in patients who present a prediabetic condition.

3. Patients who have psoriasis or other dermatoses, in which a low protein diet is often resorted to, may also be prediabetics.

4. Therefore, before a special diet, low in protein and rich in carbohydrates, is instituted, the sugar tolerance of the patient should be ascertained.

Thanks are expressed to Prof. John A. Fordyce for his permission to use the facilities of the Laboratory of the Department of Dermatology and Syphilology, Vanderbilt Clinic, New York.

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THE USE OF GENTIAN-VIOLET AS A RESTRAINER IN THE ISOLATION OF THE PATHOGENIC MOLDS

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The work of Churchman[1] on gentian-violet has shown that this substance possesses the peculiar property of inhibiting in high dilution the growth of grampositive organisms. This fact has been confirmed by Krumwiede and Pratt,[2] and applied by Petroff[3] in his medium for isolation of cultures of the tubercle bacillus from sputum. As most of the skin saprophytes are gram-positive, it occurred to us that gentian violet might be of value in restraining the growth of skin contaminants in cultures during the isolation of the pathogenic molds of the skin and hair, provided the substance should prove to be non-inhibiting for the molds themselves.

AUTHOR'S EXPERIMENTS

Technic.—A preliminary series of experiments was undertaken using four molds of widely varying growth characteristics to determine in a general way the effect of gentian-violet on their growth. The organisms, all of which were isolated in this laboratory, selected were: (1) *Penicillium* (*saprophytic*), (2) *Achorion schönleinii* (D. R. 206), (3) *Trichophyton rosaceum* (D. R. 201), (4) *Microsporon audouini* (D. R. 73). A 1-100 watery solution of gentian-violet (Grübler) was carefully prepared. This was added to tubed Sabouraud's maltose mediums (melted 10 c.c. to each tube titrated to 1 per cent acid, phenolphthalein) so as to make these dilutions: 1 : 1,000,000; 1 : 500,000; 1 : 400,000; 1 : 300,000; 1 : 250,000; 1 : 200,000; 1 : 166,000; 1 : 143,000; 1 : 125,000; 1 : 111,000; 1 : 100,000; 1 : 83,000; 1 : 71,000; 1 : 60,000; 1 : 58,000; 1 : 41,000; 1 : 20,000; 1 : 10,000; 1 : 5,000; 1 : 1,000.

The tubes were seeded and allowed to incubate at room temperature for four weeks. Slants of Sabouraud's maltose agar not containing gentian-violet were seeded as controls.

Results.—1. *Penicillium* grew through all concentrations abundantly and with no evident impairment except in the two strongest

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* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

[1] Churchman: J. Exper. Med. **16**: 1912; Churchman and Michael: Ibid.

[2] Krumwiede and Pratt: Centralbl. f. Bakteriol. **68**: 1913; Ibid., Proc. New York Path. Soc. **13**: 1913.

[3] Petroff: Johns Hopkins Hosp. Bull. **26**:276 (Aug.) 1915.

(1 : 1,000 and 1 : 5,000), in which the growth was well developed but somewhat less vigorous than in the control.

2. *Achorion schönleinii* grew up to a concentration of 1 : 71,000. No growth occurred in greater concentrations. It was abundant through 1 : 100,000 with no evident inhibition as compared with the control on the next two tubes. The growth graded downward in vigor until it was scanty on the tube representing a dilution of 1 : 71,000.

3. *Trichophyton rosaceum* grew through 1 : 41,000. Through 1 : 83,000 the growth was as abundant as on the control. The next four tubes graded downward until the growth was scanty in a concentration of 1 : 41,000.

4. The *Microsporon audonini* grew to a concentration of 1 : 166,000. The growth was scanty at the 1 : 166,000 concentration, but was good on the tube preceding, (1 : 200,000).

As to the strength of gention violet necessary to inhibit the growth of the gram positive-bacteria, Churchmann[1] says: "Four gram-positive organisims were planted in broth tubes containing gentian violet in a dilution of 1 : 1,000,000, and at the same time control inoculations were made in plain broth. In none of the violet broth tubes did growth occur." "A dilution of 1 : 1,000,000 is thus seen to stop the growth of these organisms, and their growth may be retarded even by a dilution of 1 : 2,000,000."

We have repeated the above experiment of Churchman and obtained similar results. Grown on *solid* mediums, the dilution necessary to restrain growth of staphylococci was found to be between 1 : 500,000 and 1 : 1,000,000. The nature of mold work is such that solid mediums must be used, and our figures therefore will not run exactly parallel with Churchman's.

The concentration of gentian violet necessary to restrain the growth of the four molds above indicated was therefore found to be much stronger than that necessary to restrain the growth of gram-positive cocci and bacilli.

Technic of Second Experiment.—Following this preliminary work, which seemed to indicate in a general way that the mold group was more resistant to gentian-violet than the ordinary gram-positive cocci and bacilli, a series of fifty organisms including members of the mold group, the sporotricha and actinomyces, was planted on three concentrations of gentian-violet—1 : 500,000, 1 :250,000, and 1 : 100,000.

The dilutions were made in Sabouraud's proof maltose agar from gentian-violet made by Grübler.

Results.—Cultures 1 to 28 inclusive grew on all three strengths of gentian-violet as readily as on the control with no apparent retarda-

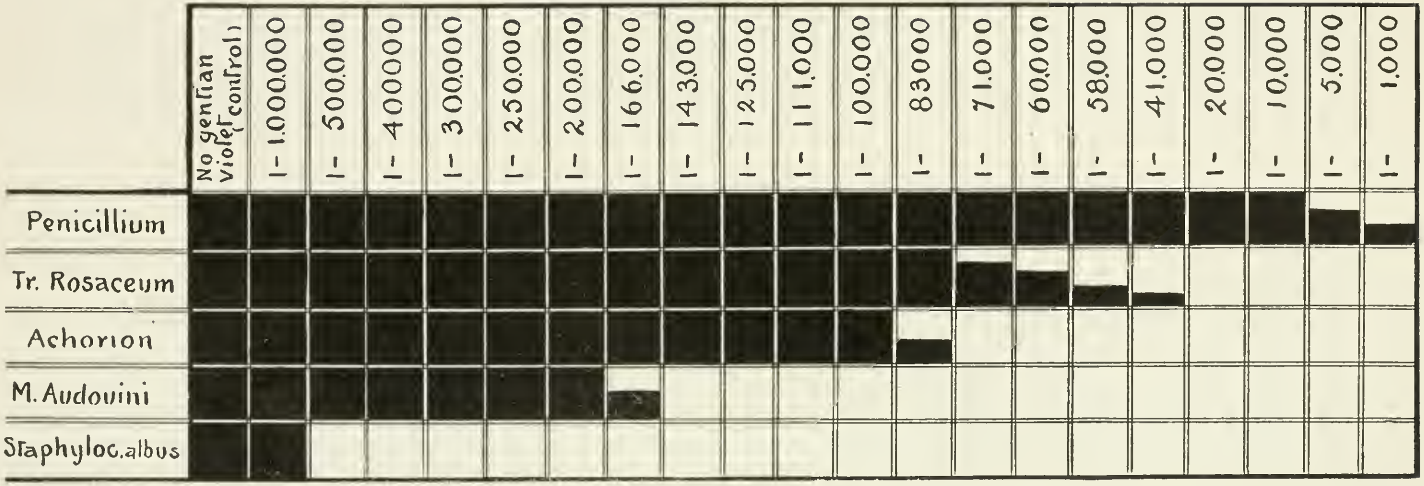

Fig. 1.—Table illustrating results of preliminary trials comparing growth of four molds with *Staphylococcus albus,* using gentian-violet at graded concentrations. The "stepped" effect is to indicate the abruptness with which luxuriance decreases as the restraining point is reached.

Organisms Used and Sources*

	D. R. No.	Source of Organism	Source
1.	(403)	Epidermophyton inguinale	U. P.—around anus
2.	(213)	Aspergillus variegatus	U. P.—nails
3.	(351)	Trichophyton gypseum	Paris—Sabouraud
4.	(253)	Trichophyton violaceum (?)	U. P.—scalp
5.	(407)	Microsporon lanosum	U. P.—scalp
6.	(336)	Achorion schönleinii	Paris—Sabouraud
7.	(358)	Penicillium brevicaule	U. P.—toe
8.	(219)	Epidermophyton inguinale	U. P.—thighs
9.	(342)	Trichophyton fumatum	Paris—Sabouraud
10.	(338)	Achorion gallinae	Paris—Sabouraud
11.	(341)	Trichophyton niveum radians	Paris—Sabouraud
12.	(344)	Trichophyton plicatile	Paris—Sabouraud
13.	(339)	Microsporon lanosum	Paris—Sabouraud
14.	(363)	Epidermophyton inguinale	U. P.—thighs
15.	(345)	Trichophyton rosaceum	Paris—Sabouraud
16.	(346)	Microsporon fulvum	Paris—Sabouraud
17.	(206)	Trichophyton album (?)	U. P.—favus scalp
18.	(201)	Trichophyton rosaceum	U. P.—leg
19.	(73)	Microsporon audouini	U. P.—scalp
20.	(86)	Trichophyton lanosum (?)	U. P.—cheek
21.	(316)	Epidermophyton inguinale	U. P.—thigh
22.	(364)	Epidermophyton inguinale	U. P.—thigh
23.	(295)	Microsporon audouini	U. P.—scalp
24.	(347)	Achorion quinckeanum	Paris—Sabouraud
25.	(212)	Microsporon lanosum	U. P.—scalp
26.	(298)	Epidermophyton inguinale	U. P.—thigh
27.	(350)	Epidermaphyton inguinale	Paris—Sabouraud
28.	(381)	Epidermophyton inguinale	U. P.—thigh
29.	(365)	Sporotrichum	K. F. M.—horse
30.	(366)	Sporotrichum	K. F. M.—dog
31.	(367)	Sporotrichum	K. F. M.—horse
32.	(368)	Sporotrichum	K. F. M.—man
33.	(369)	Sporotrichum	K. F. M.—animal
34.	(370)	Sporotrichum schenki-beurmanni	K. F. M.—horse
35.	(371)	Sporotrichum councilmani	K. F. M.—man
36.	(372)	Sporotrichum	K. F. M.—horse
37.	(373)	Sporotrichum	K. F. M.—man
38.	(374)	Sporotrichum	K. F. M.—horse
39.	(423)	Sterigmatocystis nigra	U. P.—nails
40.	(424)	Aspergillus aureus	U. P.—nails
41.	(425)	Aspergillus variegatus (T. Spec.)	U. P.—nails
42.	(426)	Aspergillus cyanicentris (T. Spec.)	U. P.—nails
43.	(427)	Penicillium nigra	U. P.—toe
44.	(428)	Keratophyton salmonica (T. Spec.)	U. P.—nail
45.	(222)	Achorion schönleinii	U. P.—favus scalp
46.	(420)	Microsporon lanosum	U. P.—scalp
48.	(422)	Achorion schöleinii	U. P.—favus scalp
49.	(430)	Keratophyton eburneum	U. P.—toe nails
50.	(1)	Actinomyces bovis	Philadelphia Veterinary School—Dr. Crocker
51.	(2)	Actinomyces bovis	Philadelphia Hygiene Lab.—Dr. Bergey

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* U. P. indicates that the organism was isolated in this laboratory; K. F. M., from Dr. Karl F. Meyer, San Francisco.

tion. The sporotricha (29 to 38) inclusive grew readily on the concentration 1 : 500,000 and 1 : 250,000 without retardation and as luxuriantly as on the control. On the strongest concentration—1 : 100,000, however, there were differences. While *Sporotrichum councilmani* 35, grew as abundantly on this concentration as on the control and with no retardation, the remaining nine were retarded, the growth developing on an average four days later than the growth on the control. After growth began, the luxuriance was little if at all less than on the control except in the case of *Sporotrichum hamburger* 33, which grew scantily at all times even on the dilution 1 : 100,000.

Cultures 39 to 49 inclusive grew on all three dilutions as abundantly as on the control and with no retardation.

The two strains of actinomyces 50 and 51 were retarded in luxuriance of growth by even the weakest dilution of gentian-violet, 1 : 500,000. While there was a growth on this dilution, it was decidedly less abundant than on the control. There was no growth at all on the dilution 1 : 100,000.

Observations were made on all cultures over a period of four weeks.

COMMENT

All the organisms used had been isolated for some time from diseased tissue and were therefore thoroughly accustomed to growth on artificial mediums.

It is possible and probable that organisms growing directly from fresh material scrapings, etc., would have a different growth resistance to gentian-violet. The question of amount of material planted also arises in this connection; that is, a pure culture of an organism planted in fairly large quantity on artificial mediums, probably has a greater tenacity of growth than a small number of isolated organisms suddenly transplanted from freshly diseased material to artificial mediums. This question, however, can only be settled by the use of mediums in routine cultures over a notable time period. This we have already entered on.

We have used gentian-violet maltose mediums in the isolation of approximately twenty strains of pathogenic molds from fresh material, with no evident inhibition of growth of the specific organisms, and with apparently distinct advantage from the standpoint of restraint of contaminants. The concentrations used were 1 : 500,000 and 1 : 250,000 in Sabouraud's maltose mediums.

A difficulty yet to be overcome arises from the standpoint of the yeasts. Henrici[4] in his work on the straining of yeasts by Gram's method makes this statement: with the Gram stain "molds stain

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[4] Henrici, Arthur T.: J. Med. Res. **30**:409, 1914.

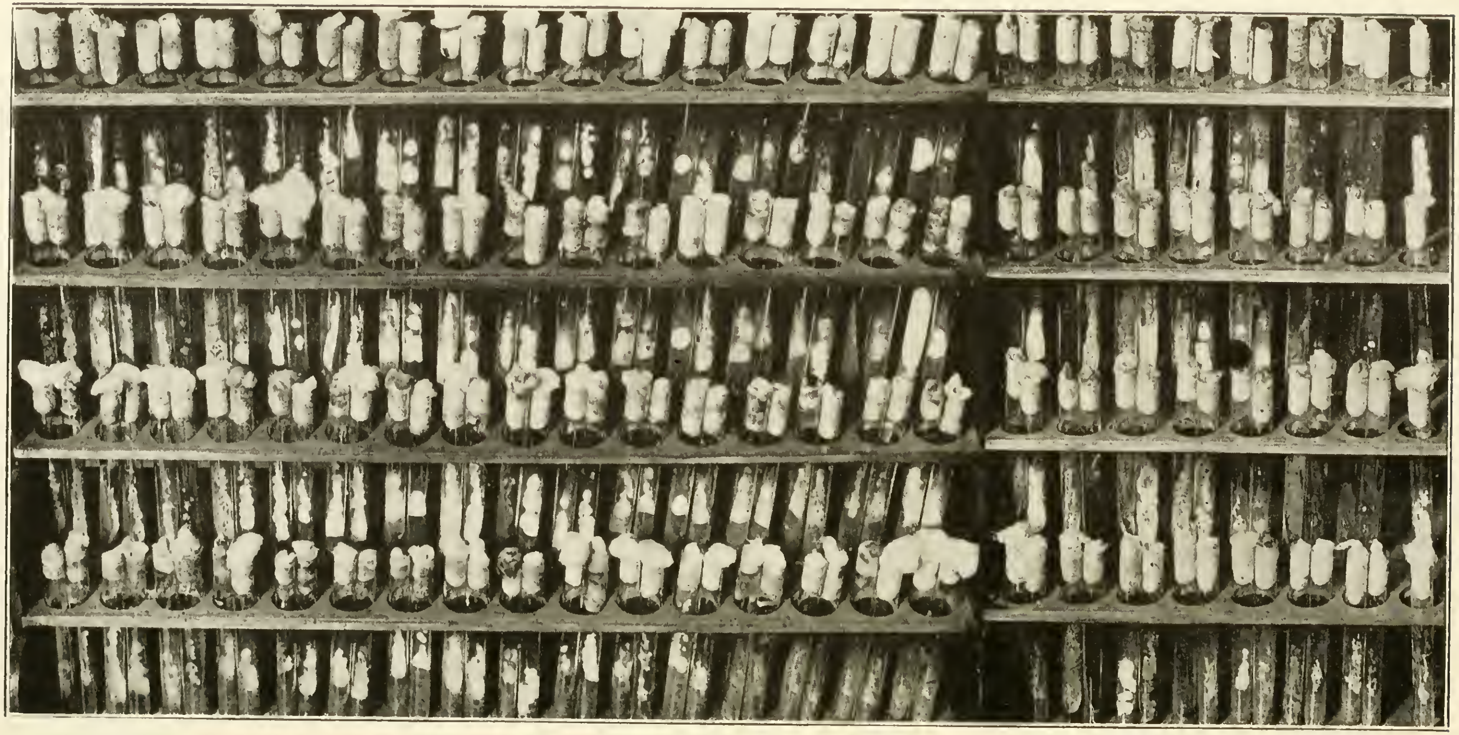

Fig. 2.—Fifty-one strains of higher organisms on three different concentrations of gentian-violet. Top row, gentian-violet 1:100,000; next row, 1:250,000; next row, 1:500,000; bottom row control—no gentian-violet.

irregularly, isolated granules in the mycelia retaining the stain while large areas do not stain at all. The yeasts and bacteria are the only classes of cells in which this property (retention of Gram stain) is frequently found. . . . As far as I know all the yeasts are gram-positive."

Yeasts are frequently a contamination in cultures from the skin. We have not yet titrated the restraining power of gentian-violet on the wild yeasts, but in routine cultures of material for the pathogenic molds the wild yeasts do not seem to have been inhibited in the 1 : 500,000 strength of gentian-violet maltose agar.

It is evident that these gram-positive organisms (yeasts) are more resistant to gentian-violet than the ordinary gram-positive cocci and bacilli and in spite of their gram-positive qualities.

The two strains of actinomyces used, while growing on the weaker dilutions of gentian-violet, yet seemed to be less resistant to this substance than the ringworm group of molds, and to be in this respect more closely related to the sporotrichi. The small number of strains used, however, does not warrant sweeping conclusions.

SUMMARY AND CONCLUSIONS

1. A dilution of gentian-violet of 1 : 500,000 in solid (Sabouraud's proof) mediums will inhibit the growth of the gram-positive bacteria.

2. Fifty-one strains of the higher organisms were found to be capable of growth on maltose mediums containing gentian-violet in as high a concentration as 1 : 250,000. This group included epidermophytons, achorions, microsporons, trichophytons, sporotricha and actinomyces.

3. The organisms above mentioned, therefore, seem to be more resistant to the restraining action of gentian-violet than the ordinary gram positive bacteria.

4. We have used a gentian-violet maltose medium (1 : 250,000 and 1 : 500,000) in the isolation of approximately twenty strains of pathogenic molds with apparently good results.

THE CULTIVATION OF EPIDERMOPHYTON INGUINALE *

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In recent issues of *The Journal of Cutaneous Diseases* difficulties encountered in the cultivation of *Epidermophyton inguinale* have been discussed. During the past two years, in the routine culture of cases of epidermophyton infection in this clinic, we have encountered the same difficulties and have to some degree overcome them.

TECHNIC

Collection of Material.—In the collection of material, precautions should be taken to minimize as far as possible extraneous contamination, especially from the saprophytic molds, which are common inhabitants of the skin surface. The skin is cleansed with 95 per cent. alcohol and allowed to dry immediately before the scrapings are taken; the knife used in obtaining scales, and the black paper into which scrapings are received, should be sterile. A large amount of material should be collected.

Time of Planting.—Mitchell [1] has suggested that scales for cultivation be allowed to dry for several days before being cultivated, in order to eliminate some of the bacterial contaminants which do not resist drying as readily as does the epidermophyton. He states that he has succeeded in growing the organism after several months of drying in the laboratory. The recent work of Dold [2] on the viability of the epidermophyton indicates that some of the strains are not as resistant to the effect of drying as has been commonly supposed. Scales from four cases were filed at room temperature in sterile envelopes and were cultured by him at intervals. One case failed to grow on the twelfth day, three on the twentieth day, and all failed to grow after thirty days' drying at room temperature. Our own experience has shown that some strains are capable of resisting drying for long periods. In a series of cultures of old material we succeeded in one case in obtaining a growth of the organism from scrapings which had been filed in a dry paper envelope one year and two months previously and in two other cases four months and five months before, respectively. However, we have also found that the epidermophyton both in cultures and in scrapings not infrequently appears to lose its ability to grow in a comparatively short time. This may be the effect of drying or some other unexplained agency, but we feel that more cultures of the organism are positive when the material is planted soon after collection.

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* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

[1] Ormsby, O. S., and Mitchell, J. H.: Ringworm of Hands and Feet, J. A. M. A. **67**:711 (Sept. 2) 1916.

[2] Dold, Herman: China M. J. **34**:34 (Jan.) 1920.

Culture Mediums and Plates.—A plate method that obviates the drying out of medium over the long periods of time necessary for mold culture, gives easy accessibility to the medium surface for planting and picking colonies and at the same time lowers chances of contamination, has been found to be more or less satisfactory and may be worthy of description in detail. Melted agar medium cooled to 45 C. is allowed to run slowly from a pipet into a Petri dish so that an area of hardened medium is formed in the center of the dish leaving a zone free of medium about it. This prevents secondary contamination from creeping in from the edges as so often happens when the entire area of the floor of the Petri dish is filled with medium.

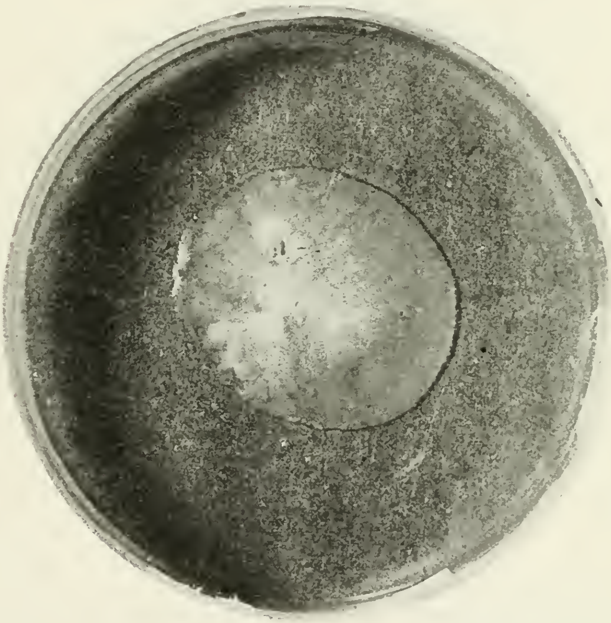

Fig. 1.—Top of culture, looking through the glass plate which serves as a cover.

As soon as the agar is well hardened the dish is inverted, the lid removed, and the half containing the medium carefully placed on a sterile glass plate 8 by 6 inches (reclaimed photo plate). Melted paraffin is then painted around the contact circle of the plate and Petri dish with a small brush thus sealing the chamber. Before planting, these modified Petri dishes are allowed to incubate at room temperature for a few days to insure their sterility, a stock being kept on hand.

Three varieties of medium have proved useful in the culture of the epidermophyton, and as a rule one plate of each variety of medium is seeded in each case.

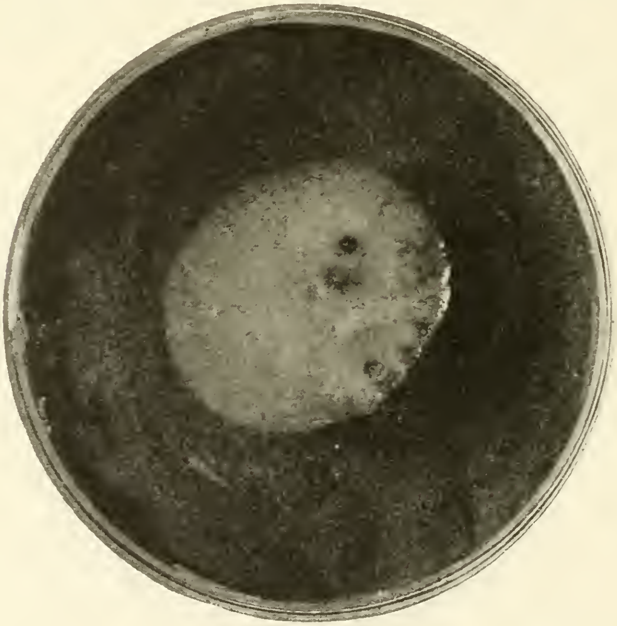

Fig. 2.—Bottom of culture. One half of the Petri dish is attached to the glass plate with paraffin.

Sabouraud's Proof Agar: This medium is made according to Sabouraud's[3] recipe. It may be worth while to call attention to the fact that most English textbooks on bacteriological technic, while specifying the amount of maltose correctly, fail to specify that the maltose must be commercial maltose and not the chemically pure product. Professor Sabouraud is emphatic in calling attention to the sparsity of growth on the chemically pure sugar medium. "Toutes les maltoses, sci-disant pures, que j'ai essayées, donnent des cultures, d'une médiocrite insigne, alors que la maltose commerciale dont je me sers donne des cultures admirablement belles et differenciées." (All the so-called pure maltoses which I have tried give cultures of a mediocre character, while the commercial maltose which I use gives cultures, very beautiful and distinctive.)

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[3] Sabouraud: Les Teignes, 1910, Paris, Masson et Cie, p. 111.

Blood Sabouraud's Medium: Human blood which has been heated to 55 C. for thirty minutes is added to Sabouraud proof agar in the proportion of from 3 per cent. to 5 per cent. and plates made as described. This medium has given us positive cultures when the first plate failed to show the organism, and we feel that it is of advantage.

Gentian-Violet Blood Maltose Agar: Churchman's[4] work on gentian-violet has shown that this substance possesses the peculiar property of inhibiting the growth of gram-positive organisms in high dilutions. In a preceding paper we have published the results of preliminary experiments on the effect of gentian-violet on four members of the mold group of widely varying cultural characteristics, which seemed to indicate that gentian-violet exhibited its restraining effect in much higher dilution on gram-positive organisms than on the mold group. We have applied this in the culture of epidermophyton, which is apparently not at all inhibited in the dilution of 1:500,000, which is sufficient to inhibit the gram-positive organism.

In practice a 1:100 watery solution of gentian-violet (Grübler) is kept as stock. A 1:10,000 dilution is made by adding 0.1 c.c. of the stock to 9.9 c.c. of distilled water, 0.2 c.c. of this dilution is added to 10 c.c. of Sabouraud's proof agar, making a final dilution of 1:500,000. Blood is added to this medium in the proportion outlined and the medium plated. The agar should be free of phosphatic sediment as the sediment takes up relatively large amounts of the dye and thus interferes with the proper dilution.

Seedings: A large amount of the scrapings is planted on each plate. This is an important point.[5]

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[4] Churchman, J.: J. Infect. Dis., 1912.

[5] In addition to the references already given, the following may be of interest:

White, C. J.: J. Cutan. Dis. **37**:501 (Aug.) 1919.

A NOTE ON THE DISSEMINATION OF SPIROCHAETA PALLIDA FROM THE PRIMARY FOCUS OF INFECTION *

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NEW YORK

Although it is now generally recognized that the time during which a syphilitic infection remains confined to the primary focus of entry is comparatively short, and that the effort to distinguish between a localized and generalized stage of infection is largely an arbitrary one, no one has shown just how rapidly the infecting organisms may spread after they have once gained entrance to the body or when a generalized infection may be said to have occurred. These are questions of obvious clinical importance and considerable light may be thrown on them by the sequence of events which follows local inoculations of *Spirochaeta pallida* in the rabbit.

In a recent series of experiments, an attempt was made to obtain some data on these points by a systematic determination of the presence of spirochetes in the inguinal lymph nodes and the circulating blood of rabbits at various intervals after scrotal or testicular inoculation.

The organisms used in these experiments were old strains, one of which was isolated by Nichols and Hough in 1912 and the other by Zinsser and Hopkins in 1913. They have been maintained in rabbits for periods of nearly seven and eight years.

TIME OF INVASION OF THE REGIONAL LYMPH NODES

The method used for determining invasion of the regional lymphatics was the excision of the inguinal nodes (under ether anesthesia) of rabbits that had been inoculated by the introduction of a small bit of infected tissue beneath the skin of the scrotum and the injection of an emulsion of these nodes into the testicles of normal rabbits. In all, inguinal nodes from twenty-nine rabbits were examined by this method.

The first series of examinations was made on rabbits showing definite primary lesions and well marked lymphadenitis in order to test the method on cases in which infection and involvement of the regional lymphatics were both apparent. The period covered by this series of examinations was from sixteen to sixty-one days after inoculation, and spirochetes were demonstrated in the nodes of all these animals.

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* From the Laboratories of the Rockefeller Institute for Medical Research, New York.

With this data available, the time between inoculation and excision of the nodes was then progressively reduced to seven, five and two days. These periods were again fixed with reference to pathologic changes. The five and seven day periods corresponded roughly with the time at which definite enlargement and induration of the inguinal nodes could nearly always be recognized, but usually antedated the appearance of the initial lesion, while little or no alteration could be detected in the nodes within the first forty-eight hours.

There were twenty-three animals in this group. In two cases (seven days), spirochetes were demonstrated in the nodes by dark field examination and no inoculations were made from this material. The other nodes all gave positive results by animal inoculation, thus showing that extension of the infection to the inguinal lymph nodes antedated both the appearance of the initial lesion and the occurrence of definite alterations in the nodes themselves, and that this occurred constantly within a period of less than forty-eight hours from the time of inoculation.

INVASION OF THE BLOOD STREAM

Supplementing the observations on invasion of the lymphatics, a series of experiments was carried out to determine the time and frequency of blood stream invasion. The mode of determining the presence of *Spirochaeta pallida* in the blood was by bleeding from the heart, defibrinating and injecting 0.5 c.c. of blood into the testicles of normal rabbits.

In the course of these experiments, a large number of bleedings was made covering the time from the appearance of the initial lesion (twelve to fourteen days after inoculation) through various periods of its development, with the result that spirochetes were shown to be constantly present in the circulating blood by the time an infection could be recognized at the point of inoculation.

A small series of animals was then bled arbitrarily at an interval of one week after inoculation and it was found that even as early as this spirochetes were sufficiently numerous in the circulating blood to produce infection when amounts as small as 0.5 c.c. were injected into the testicles of normal rabbits.

THE ESTABLISHMENT OF A GENERALIZED INFECTION

In view of the results obtained from examinations of both the inguinal lymph nodes and the circulating blood of infected animals, there seemed to be no real object in attempting to determine more exactly the time at which spirochetes could be recovered from either the lymphatics or the blood stream. However, there might be some legitimate question as to whether a dissemination of spirochetes, such as had been shown, could be regarded as a true generalized infection. In order to settle this point, ten rabbits were inoculated in the right scrotum only and forty-eight hours later the entire scrotum and testicle of this side were amputated under ether anesthesia. In spite of the complete removal of a wide zone of tissue surrounding the area of inoculation, all of these animals developed syphilitic lesions, thus showing that true infection of parts outside of the zone of operation had taken place within the brief period of forty-eight hours.

CONCLUSIONS

While the conditions of these experiments are not entirely analogous to those that obtain in cases of human infection, the general course of events is undoubtedly much the same in the two cases.

It would appear, therefore, that, for practical purposes, there is probably no appreciable time during which a syphilitic infection can be regarded as confined to the focus of entry but that, immediately infection takes place, the spirochetes begin to multiply and invade the surrounding tissues, gaining access to both the lymphatics and the blood stream, and are widely distributed over the body even before an initial lesion can be detected.

The early appearance of a distinctive lesion at the site of infection and the lapse of time required for the development of generalized lesions are to be viewed more as a result of a sequence in localization and concentration of spirochetes at given points than as indications of the time required for their dissemination.

THE CLINICAL APPROACH TO SYPHILIS, WITH SUGGESTIONS FOR ITS REVIVAL AND DEVELOPMENT *

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For the past four years, a large part of my time has been occupied with the development of clinical interest in syphilis in the diagnostic group of the Mayo Clinic, through whose hands pass approximately 60,000 patients a year. In developing a diagnostic and therapeutic approach to the disease I have been compelled to give constant and intense thought to the present and future possibilities, limitations, and tendencies of syphilology as a special field of medical activity. As a dermatologist, I may be pardoned for bringing before you for your criticism and suggestions some of my impressions and perplexities. I have passed through a period of misgivings and distrust of the possibilities of the work, engendered in part by the confusion and lack of cooperation which at first sight appears to pervade the field, and in part by the feeling that the clinical syphilographer as such reached his culmination in Fournier and that others who in these times essay the rôle can be no more than base imitators. In the grip of that depression I cast yearning eyes on the laboratory, as many a better man has done, and longed for the day when with a corps of trained routinists to buttress me against the demands of patients, I could indulge in a species of endowed reflection in sequestration, and in animal experiment. From this monastic phase I am slowly emerging in response to a new appreciation of the enduring worth and ultimacy of clinical research.

The critical problem of the next half century of syphilology, as it has appealed to me during the past several years, is not so much the extension of the laboratory knowledge now so highly developed, as the application of the knowledge already existent, to the pressing clinical problems of the disease. No reasonable man would seek to minimize the worth of the laboratory contribution, whose fundamental character needs no discussion in this assembly. But a decade of transformations has been superimposed on the clinical syphilology of Fournier, Hutchinson and Morrow as two fluids of different densities may be superimposed the one on the other in a test tube. I believe that there has never been a greater need for clinical revision of laboratory specialization in the diagnosis and treatment of syphilis. The Was-

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

sermann reaction is passing from the phase of uncritical acceptance to one of almost reactionary distrust. Adequate examination of the spinal fluid has transformed our conceptions of neurosyphilis, and the postmortem identification of the *Spirochaeta pallida* in the tissues of treated and supposedly cured syphilitics has compelled a much needed return to conservatism in our therapeutic enthusiasm based on modern chemotherapy. In helping to make the clinical readjustments for which the need is so pressing, it seems to me that man may yet aspire to the laurels of a Fournier. The field of clinical syphilology, instead of being closed, has just been thrown open anew.

My struggles to become in more than name the syphilographer of the Mayo Clinic, epitomize, I believe, something of the course which clinical syphilology must run in the next few decades, much as the ontogeny repeats the phylogeny in von Baer's law. Coming to my work primarily as a dermatosyphilographer, I found myself confronted point blank with phases of the disease with which my acquaintance was of the remotest. To witness the completeness with which syphilis of the stomach had been worked out by the men whose colleague I became, to learn of diagnostic signs such as neurogenous bladder whose existence I had never suspected, was an experience calculated to remove every trace of the bumptious from my conceptions of my position. Consciously or unconsciously the diagnostic group of the Clinic taught me syphilology in at least as full a measure as I taught them. They have taught me so effectually that I am all but a convert to the belief that the future of modern syphilology is in the hands of the group and that the day of the syphilographer who can combine in his sole personality both the technical attainments and the wealth of general and detail knowledge that make him a master of the disease, is past.

Appreciation of the complexity of the procedures, on which the modern intensive study of clinical syphilis depends, grows on one as his experience with group practice develops. For my own information I recently summarized the list of examinations on which at one time or another my department relies for a diagnosis or information on the status of a syphilitic infection (Table 1). This complex instrument involves the most extraordinary range and combination of structural and functional tests imaginable. As one's facilities for employing it extend and one's acquaintance with the instrument develops, he appreciates more and more how illusory is the hope that syphilis will ever yield to a single diagnostic key. Yet it is precisely this search for a touchstone in syphilis as in other diseases, which in this day betrays the large body of medical practitioners into an unthinking, if temporary, worship of single procedures such as the Wassermann reaction and the luetin test.

TABLE 1.—THE MULTIPLE PROCEDURE DIAGNOSTIC ATTACK ON SYPHILIS

1. Intensive study of the anamnesis
2. Social estimation of the case
3. Study of the family both in history and examination
4. Serum Wassermann reaction (single antigen)
5. Modifications and intensifications of the serum Wassermann test, such as the provocative, cold fixations, multiple antigens and Wassermann series
6. Examination of the cerebrospinal fluid (two Wassermann tests, Nonne, cell count on the fresh fluid, colloidal gold test)
7. Darkfield examination and stains of fresh secretions
8. Luetin test
9. Levaditi and other tissue stains
10. Neurologic examination
11. Eye examination
12. Ear examination
13. Nose and throat examination
14. Dermatologic examination of the skin and mucous membranes
15. Visceropathic studies of the liver and spleen, and of the stomach, involving the study of anemias, blood dyscrasias, test meals, esophagoscopy, roentgen examinations and so forth
16. Special cardiovascular examination, including the physical findings, blood pressure, electrocardiographic examination, and so forth
17. Roentgenologic examination
18. Exploratory operative procedures (seldom used until after the therapeutic test)
19. Genito-urinary examination
20. Therapeutic test
21. Necropsy

The rapid modification of the clinical knowledge under the pressure of new technical diagnostic and therapeutic methods has induced a peculiar state of disorganization in the syphilologic realm. True syphilology is for the time being lost in the mazes of an analytic era and the syphilologic workshop is crowded with personalities each so intent on the part which he contributes that he can give no thought to the whole. It comes about, therefore, that in the search for a syphilologist one encounters instead of the single master an astounding procession of partial personalities and hyphenates: the interno-syphilographer, the sero-, the neuro-, the dermato-, the gyneco-syphilographer, the syphilo-therapist and syphilo-pathologist, even the ophthalmo- and oto-syphilographer, and last, though far from least, the genito-urinary or penile syphilographer. The syphilologist of the future is as yet in a phase of mental dissociation suggesting the unfortunate condition of the Miss Beauchamp of Morton Prince's[1] study. Unless some means can be found to synthesize a single personality from the existing parts, Fournier will indeed have been the last of the great masters.

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[1] Prince, M.: The Dissociation of Personality, New York, Longmans, 1906.

The problem of today, then, in syphilology is to introduce a synthesist among the analysts, and to provide the workshop of syphilology with an assembler as well as with makers of parts. My experience, such as it is, has all but convinced me that in the development of coordinators rather than performers of new technical tests lies the really great opportunity in this field of medicine.

THE IDEAL SYPHILOGRAPHER AND SYPHILOLOGIC SERVICE

I confess that I do not see how it is possible for one man to unite within himself both the powers of synthetic interpretation and of detailed technical performance which modern syphilology requires. In his effort to become a syphilographer, therefore, our future Fournier must in a measure, it seems to me, choose between technical proficiency and intellectual grasp of principles. Ability to perform an irreproachable Wassermann test, to examine the fundus of the eye, to carry out a complete neurologic examination or to cystoscope a bladder may be graces of accomplishment, but I believe that they subside into secondary importance in comparison with the vital need for a tremendous breadth of outlook on the disease. By his coordinating power, by his just appreciation of the worth of each single test and manifestation, and yet of the immeasurably greater possibilities of the interpreted whole, the syphilographer of the future will stand or fall. He will be that type of clinician whose success will be measured to no small degree by ability to secure the hearty good will and cooperation of colleagues. Having secured it, he must be able to focus to a point their individual proficiencies in special procedures, which if they were employed alone or in discordant competition would defeat the issue.

The search for a syphilographer, and the training of one, becomes, therefore, essentially the finding and development of a certain type of man. It is unquestionably desirable that he should have exhaustive training in one or more of the special contacts which syphilis makes in medicine. He must at least also have speaking acquaintance with all the elements of his work, or he will be a narrow expounder and a poor cooperator. The point I want to emphasize, however, is that it is personality and breadth of viewpoint, not the dermatologic or the urologic or the internomedical training, that make a syphilographer. Nothing so becomes a true syphilographer, it seems to me in these days, as humility and the willingness to seek aid from experts whose acquaintance with the borderline of syphilis within their special fields may perhaps be greater than his own.

Many of you, I fear, will accuse me of reducing the syphilographer of the future to a hopeless parasitism on associates. Such a parasitism might perhaps develop were the syphilographer to confine himself merely to a judicial interpretation of the work of colleagues. In order to keep himself fresh and to retain that enthusiastic interest in the disease which is the first essential to the inspiring of others, the true syphilographer must have and preserve his forte or specialty as he extends his experience. Happy is that syphilographer whose forte encourages objectivity, keenness of observation and the ability to weigh dispassionately and decide quickly. For these four qualities, which have so much in common with the essentials of success in every life activity, no technical proficiency in examination or manipulation can ever serve as substitute.

It is because I have believed that the dermatologic training at its best develops and fosters these qualities, that I have always been partial to the dermatologic forte for the syphilograhper. It is also because I have come to realize how impossible it is for any one special group in medicine to annex syphilology as a perquisite that I have mentioned in an emphatic way how much the Mayo Clinic itself contributes to my personal development along syphilologic lines. I am filled with enthusiasm for the amount of syphilology that can be learned and taught in the course of modern routine medical and surgical diagnosis. You will, I am sure, pardon my perhaps over-ardent advocacy of the group diagnostic attack on syphilis. I cannot but contrast with it my own situation as an isolated unit, when in the effort to live up to the responsibilities of a syphilographer I, in company with the other hyphenates and partial personalities, wielded fragments of the potential syphilodiagnostic and therapeutic machine as if all other parts were nonexistent. Such an experience makes one sympathetic with the problem of the general practitioner in the diagnosis of syphilis, as he gropes with his Wassermann lantern through the dense forest of spirochetal possibilities.

Appreciation of the problems I have brought up has a practical bearing on the way in which one attempts to develop the clinical approach to syphilis among his confrères. To this problem there are many aspects beside the principle of exclusive title to the treatment of all patients with syphilis, about which the controversy usually seems to rage. Personally I believe that the ideal syphilologic service is not created by any fiat of hospital or medical school authorities but by the personality which is essential in the makeup of the syphilographer. The man whose conception of syphilologic progress consists of personal aggrandizement will probably make himself lasting enemies by his efforts to absorb the serology, the roentgenology, and the various other special aspects of the diagnosis of the disease. A much more ideal condition is created, it seems to me, when the would-be syphilographer, whatever his forte, gains his following by the spontaneous recognition on the part of his confrères of his enthusiasm and his special equipment for his post.

It will be apparent from what I have said of the syphilographer of the future, that organizing duties will form no small part of the field for the exercise of his energies, and that a recognition by the partial syphilographer of today of the salient responsibilities which his successors will inherit, will do much to lighten their task of creating a new clinical syphilology. Five major duties rest on those of us who raise the cry in the wilderness, "Prepare ye the way".

DUTIES TO BE PERFORMED IN CREATING A NEW CLINICAL SYPHILOLOGY

The first duty is to lift syphilis, the object of our interest, from the field of routinism. Routine interest, or perhaps routine lack of interest, is the curse of all large medical organizations. Some of the poorest syphilologic diagnosis in the world is, to my mind, the product of the routine Wassermann test on patients entering hospitals. Even though the quantitative yield of recognized syphilis be large by such a procedure, and even though it may be an ultimate desideratum to inaugurate a modified routine system, it deserves only secondary, and not the primary emphasis usually accorded it. Routine procedures discourage the alert suspiciousness of mind and zest in ferreting out the disease that is a fundamental attribute of the true syphilographer, and which he must develop to the highest possible degree in his clinical cooperators.

Ferretting being so large a part of the work of the syphilodiagnostician, his second duty is to inspire associate ferrets, so to speak, in the form of fellow clinicians, who can be specially interested in particular aspects of the general problem. Nearly every medical examiner in a group can hear a heart murmur. Usually only one in a group cares to develop to its utmost detail the art of recognizing the earliest manifestations of cardiovascular syphilis. To have the personal gift and the ability to present the problem of syphilis to a colleague so as to inspire him to contribute his diagnostic acumen to the study of some particular aspect of the disease is one of the hall marks of a successful developer of the new clinical syphilology.

The third duty of a syphilographer as I conceive it, and one well calculated to compel a judicial frame of mind and a wide acquaintance with the disease, is that of developing means of checking the results of individual diagnostic, therapeutic, and research procedures against each other and against the general knowledge of the disease which develops as a result of such experience. The syphilologic service thus becomes a clearing-house for information and opinion and a court of last resort in diagnostic decision. As its presiding officer, the syphilographer is under obligation to formulate the experience of the court at frequent intervals, in as concise and conclusive terms as possible. With this end in view my own department, in addition to its formal publications, issues at frequent intervals, a house letter, which aims to epitomize current progress in the field covered by the Section of Dermatology and Syphilology.

Duty number four of the syphilologic pentalogue is to make impressionism and intuitive diagnosis take tangible form and exact expression so far as possible. Diagnostic instinct in particular, so often summarized in the slang term "hunch," only too often perishes with its possessor, leaving the next generation to develop it anew. Medicine in general, and diagnostic syphilology in particular, possesses all too few of those landmarks of synthetic thinking in the form of exact, almost mathematical expressions of great principles, which adorn the more exact sciences, such as organic chemistry and physics, and which are familiar in bionomics and actuarial science. This problem of developing a mathematical and statistical syphilology is intimately connected with the last item of the pentalogue.

The mastery of data, the fifth duty, is one of the most practical and at the same time, I believe, one of the most pressing of the obligations of those who are preparing the approach to a new clinical comprehension of syphilis. The matter of records is a live one in every field of medicine. Not more than a month ago I received a letter indicating that general attention is already beginning to focus on this question in connection with the venereal diseases. On an adequate system of record quite as much as on acuity of observation, we must depend for the great body of facts and the means of detecting their interrelations which seem so conspicuously lacking in the disorganized syphilology of the present day.

There is no better exercise in humility than after four years of effort terminating in the formulation of a policy such as this, to look back on the undone in the light of one's accomplishment. To this wholesome discipline I have endeavored to subject myself during the past six months in an extended search of the records of my department for evidence of the success or failure of my policies. That I had only half envisaged the problem, in at least one of its aspects, became apparent when I was forced to discard outright nearly a thousand of the records collected during the first two years of my work. Each new effort to meet the situation has, however, brought to light new suggestions and experience to apply toward the development of the program. I would like to present briefly some of the ideas developed by such a review.

THE PERSONAL EQUATION IN INTERPRETATION OF CLINICIAN

No individual clinician is living up to the obligations of his work who is not questioning himself searchingly from time to time as to the personal equation factor in his interpretation and the consistency and logical development of his thought. The same obligation rests on one who endeavors to focus through his department the diagnostic and investigative work in syphilis carried on by his team mates. Consciousness of this obligation has been at the background of my own repeated insistence on the need for personal acquaintance with the serologist and the serologic technic underlying the Wassermann test which one employs. In these days of Wassermann enthusiasm it takes considerable courage to face a group of clinicians with the assertion that a positive Wassermann reaction is false because absolutely nothing else can be found to substantiate it. Such assertions about the negative Wassermann reaction have of course become commonplace. It is a pleasure to see in recent publications a growing tendency to recognize that the positive reaction has an appreciable margin of error which increases in direct proportion to the sensitiveness of the technic. Even the serologist is not free from subjective interpretation and is prone at times to assume title to a degree of clinical judgment which he does not possess.

Subjective interpretations and hence personal equation constantly enter into the decisions of every type of clinician regarding the advisability of making a special investigation for syphilis. Not a few of these interpretations rest on the syphilology of the past generation and the worse than incomplete teachings of even the good medical schools. Each of us unconsciously carries in his mind a few syphilologic *ipse dixits* such as "pupillary irregularities mean syphilis" and "lowered bone conduction is pathognomonic," "interstitial keratitis always involves the other eye," or "ununited fractures have no relation to syphilis." The syphilis in these rules of thumb is often the old time syphilis recognized only when there is a history of every visible accompaniment of the infection, or it is the Wassermann bound syphilis of the last ten years. It is too easy in these days to forget or not to know that there may be syphilis apparent to a neurologist which a rhinologist may never recognize and which consequently never enters into his calculations. There is also, conversely, a catch-basket syphilis which like "rheumatism" serves as a convenient place for the obscure and puzzling manifestation, whether or not due to syphilis. In both cases a partial outlook on the disease leads to erroneous generalizations, which, when announced *ex cathedra* by a clinician with a positive manner, create diagnostic flurries that require much laborious effort on the part of a true syphilographer to evaluate and perhaps correct. One of the most famous or perhaps better, infamous of *ipse dixits* of the type I mean, was the endorsement of sodium cacodylate by an otherwise brilliant surgeon, a piece of unqualified impressionism which has done untold harm and will require even greater labor than Cole[2] has expended on it, to correct. The evaluation of subjective interpretations and the struggle against a tendency to clinical dogmatism, both in himself and his confrères, must absorb a considerable portion of the energy of a true syphilographer.

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[2] Cole, H. N.: A Study of Sodium Cacodylate in the Treatment of Syphilis, J. A. M. A. **67**:2012, 1916.

I have already suggested the importance of lifting syphilis from the dead level of routine consideration or lack of it. This is what I call raising the index of suspiciousness in oneself and in one's diagnostic group. A definite pitfall awaits the worker on this phase of the problem. There is unquestionably a hypersuspiciousness, well illustrated by a case which I saw at one time with Dr. Pusey. A young man with a herpes progenitalis had sustained Wassermann tests and darkfield examinations, *ad lib.,* two spinal punctures, a circumcision and a biopsy on the glans penis, in the effort to make a syphilitic out of him. By the time this unfortunate victim of hypersuspiciousness reached the care of the distinguished conservative who finally set him right, he was in a mental state beyond description. On the remains of his glans penis he bore a recurrence of as obvious a herpes progenitalis as a dermatologist could imagine. The inevitable subjectivity of even our most important intuitive diagnosis, the recognition of the facies of hereditary syphilis, has also its amusing side. My associate brings to me an only child asking me to pass on the boy's appearance. I fail to get the intuitive impression, and so express myself. My associate then requests the boy to open his mouth and demonstrates to me the cicatricial deformity of the nasopharynx so frequently seen in association with late syphilis. The boy closes his mouth and stands before me transformed in appearance by my subjective inner mind. I seem to see his face studded with the stigmas whose existence I repudiated but a moment before. Subjectivism and impressionism can creep unconsciously into the most unsuspected angles of the most cold blooded statistical research. In my mention of records I shall point out how essential it is, therefore, to secure automatically and without prejudice certain data that satisfy the requirements of scientific control. I[3] published during the past year a deliberate check on an impression with regard to syphilis in railroad men. The statistical investigation, which was carried out on cases about which there had been no presuppositions, seemed to demonstrate a peculiar prevalence of neurosyphilis in this social group. Knowing the intense nervous strain to which most of them are subject I embraced with enthusiasm the seeming etiologic relationship and indulged in rash, though fortunately not published, expressions on the occupational factor in the course of syphilis. A subsequent investigation of farmers, now in progress, has abruptly checked my enthusiasm. Preliminary indications are that neurosyphilis will be as prevalent in this wholly different occupational type as among railroad men. Is it then a neurotropic civilization or a neurotropic spirochete that underlies the situation, or will my etiologic dream evaporate into the commonplace explanation that neurosyphilis is the least familiar aspect of the disease to the general practitioner, and for that reason the one most likely to reach a syphilographer associated with a last resort diagnostic clinic? Conjugal neurosyphilis, another example of pseudo rarity due to impressionism, in its day stood out "like a lighthouse," to use Pusey's [4] effective phrase. I suspect that it will subside into a commonplace under the diagnostic attack of the new syphilology, which has so many ways of demonstrating early neurosyphilis, that the person with syphilis, whether husband or wife, who escapes the demonstration of some involvement of the nervous tissues, will be the exception rather than the rule. May I align one more aspect of impressionism with those that have gone before? I refer to impressionism in syphilotherapy, with special reference to the fact of cure. In preparation for a hearing before a congressional committee, in which I expected to be examined on the minimum of treatment necessary for cure, and in which I had prepared the usual anathema for mouth medication and the usual panegyric in favor of arsphenamin, the spirit moved me to check up my stock phrases with a little study of my own records. The study was an abortive one, rendered abortive, not by lack of interesting findings, but by the glaring defects of the ordinary system of record. We carried it far enough, however, to make us realize that some patients attained clinical cure on so little and some others go on to the gravest complications on so much, that the last thing a true syphilographer would dare to do would be to dogmatize on therapy and cure.

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[3] Stokes, J. H., and Brehmer, Helen E.: Syphilis in Railroad Employees (A Clinical Study of an Occupational Group), J. Indust. Hyg. **1**:419, 1920.

OBJECTIVE INTERPRETATION OF THE DISEASE

The obvious remedy for situations such as I have described lies in recourse to the objective as distinguished from the subjective interpretations of the disease. Syphilis is a disease with a low subjectivity and a high objectivity. Yet in this field also one encounters the gravest of problems. Objective tests for syphilis consist essentially of examinations for structural and for functional changes, the one type naturally merging itself at times in the other. The standard of reference for the structural tests must be the visible norm determined by experience. Visible conceptions of the normal are the easiest to obtain and, like all visual impressions, have a satisfying degree of concreteness. It is precisely the possession of visible interpretative norms which gives the dermatologist and ophthalmologist their opportunities for syphilologic diagnostic éclat. Just as most people have visual memories and visual standards of judgment, so the visual norm in syphilologic diagnosis is the safest, and tests in which something can be seen are among the major assets of the syphilographer.

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[4] Pusey, W. A.: Syphilis as a Modern Problem, Chicago, American Medical Association, 1915.

Nonspecificity in tests for structural change places a distinct qualification on their value. The weaknesses of such tests are apparent in the physical diagnosis of abdominal lesions, and in the roentgenologic picture of syphilis of the lung, and at times in that of certain bone changes such as periostitis, in which there seems to be doubt as to whether a true syphilitic picture exists. The electrocardiographic study of the condition of the myocardium thus far at our hands has yielded largely nonspecific results. The evaluation of the degree of nonspecificity in a test for syphilis can only be accomplished by a search for collateral evidence and it is precisely in this direction that the true syphilographer should be of the greatest service.

The functional test for syphilis is rendered more uncertain and confusing in interpretation by the difficulty of establishing a definite norm in the absence of visible changes. A definite norm and standardized conditions of performance are just as essential parts of the interpretation of syphilologic functional tests as they are of structural tests. We have had opportunity to appreciate the confusion which a lack of functional norms may introduce into the interpretation of tests for syphilis in our study of bone conduction in the diagnosis of the disease, in the interpretation of the Bárány tests for inflammatory changes in the brain stem, and in our comparison of records of various observers on the behavior of the pupil. In our work on bone conduction,[5] for example, it was found that under standardized conditions reductions up to four seconds, formerly accepted by some clinicians as almost pathognomonic of syphilis, are within the normal range of variation of the test, and that complete analysis of the results placed still further qualifications on its diagnostic value. The importance of standard conditions for the performance of pupillary reaction tests becomes apparent when the complexity of the mechanism and the factors influencing the response is considered. The neurologic examination itself is a conspicuous example of multiple functional tests for structural abnormality. It derives its value from the fact that the individual parts of the multiple procedure serve as checks on each other. There could be few better patterns after which to model the syphilologic diagnostic machine than the complete neurologic examination.

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[5] Goeckerman, W. H.; Barlow, R. A., and Stokes, J. H.: The Diagnostic Value of Lowered Bone Conduction in Syphilis, Am. J. Syph. **3**:240, 1919.

GROUP WORK AND MULTIPLE PROCEDURE IN SYPHILOLOGY

After such an elaborate analysis of the problem of syphilologic diagnosis and clinical interpretation I may be pardoned if I raise one more question. Is the value of individual experience with the disease as a whole lost by group methods of investigation, and does the scattering of the problem through a number of personalities multiply the subjectivity and personal equation factors to the point where the results become unreliable? An incidental type of answer to this question appeared in the course of the study of syphilis in railroad men already referred to. The original statistical analysis was based on a group of fifty cases taken at random from the files. In offering the study for publication I was rebuked by an editor for presenting conclusions based on insufficient data. In order to vindicate my confidence in the ability of the diagnostic group to paint with accuracy the clinical picture of syphilis from a comparatively small number of cases, I compared with the first group a second group of fifty unselected cases taken from the files (Table 2). The parallelism of the results appears to me to be a vindication and an index of the accuracy and consistent quality of group work in syphilology. It seems after all not unreasonable that the increased exactitude of tests performed by specially trained men will more than compensate for some increase in subjectivity, and that the checking of the personal equation of one against that of the other will greatly reduce rather than increase the ultimate importance of this factor.

Multiple procedure in the examination of syphilis makes life anything but easy for the syphilographer, whose lot it is to carry his work through the complex interpretations that underlie diagnostic and therapeutic decisions. Subconscious reasoning and temperamental factors inevitably enter into the work of synthesis. Given a childless young married woman with a positive Bárány finding, indicating a diffuse lesion in the brain stem, a single ++ Wassermann reaction in a provocative series of seven tests, a bone conduction of — six seconds, and negative spinal fluid, a history of a father who died abruptly of heart failure and relief of dizziness on therapeutic test with a subsequent relapse under inunctions. What is to guide me, in the absence of facies and stigmas, to a diagnosis of obscure heredosyphilis? In one mood my intuitive sense that something ought to underlie such a complex might lead me to ask for an examination of the patient's mother and sister, to find confirmed in them my suspicions as to the nature of the process in the original patient. On another occasion a correct solution might wholly escape me. On still a third occasion a fortuitous necropsy might send my card house of suspicions tumbling about my ears. To decide just which of a complicated group of findings deserves major consideration; just how much weight each

TABLE 2.—Comparison of Duplicate Surveys of Two Groups of Fifty Railroad Men Each *

	Percentage	
	First Series	Second Series
Cerebrospinal fluid positive	64	79
Lues, central nervous system	79.5	83
Lues III, cardiovascular	18.7.	20
Blood Wassermann negative	57	58
Blood Wassermann positive	43	42
Wassermann weak positive	4	2
Use of alcohol	75	61
Heavy drinkers	36	33
History of lues II unobtainable	62.5	60
Lues recognized at some time	55	57
Age of onset of late symptoms—over 30	78	75
Gonorrheal history positive	80	73
Gonorrhea only	24	19
Symptoms appearing from six to twenty years after infection	71	67
Per cent. infected by the age of 32	91	81
Wassermann on men under 25 will reach	70	60
Sterile or pathologic marriages	44	50
Age on entry—patients between 25 and 40	32	36
Concerned in operation of trains	76	70
Concerned in operation of engines	36	36
SYMPTOMATOLOGY		
Gastric	28	22
Not suggestive of lues	18	24
Headaches and head pains	16	16
Cardiac	14	16
Diplopia and poor vision	14	10
Malaise, weakness	12	8
Shooting pains	10	20
Bladder (subjective)	10	4
Nervousness	8	4
"Do I have syphilis?"	8	6
Laryngeal	8	6
Rheumatism	4	18
Ataxia (subjective)	4	6
Girdle pain	4	4
Dizziness	2	8
OBJECTIVE EXAMINATION		
Abnormal knee reflexes	65.1	79
Abnormal Achilles	78.1	62
Romberg positive	38	42
Speech defect	15.7	17
Mental symptoms	38.4	38
Paresthesias	55.8	51.3
Ataxia (objective)	36.8	36.3
Bladder (objective)	47.5	20.5

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* Reprinted from J. Indust. Hyg. **1**:419, 1920.

is entitled to in making the final decision, and at just what point clinical syphilis may be considered to cross the threshold of identification in an obscure case, presents problems that are unsurpassed in difficulty and in fascination. In time we shall, I hope, by careful statistical evaluation be able to give mathematical expression to some of the elements of the intutitive synthetic instinct and perhaps with a slide rule or formula arrive at some approximation to a diagnosis, much as Dreyer[6] obtains an estimate of the prognosis in tuberculosis by a mathematical computation based on vital capacity.

One of the most interesting impressions one gathers from constant use of multiple diagnostic procedure is that of the extreme rarity of monosymptomatic or truly latent syphilis. In connection with this point we have just completed a survey of an unselected group of Wassermann-fast cases. The polytropism of syphilis, so to speak, stands out strikingly in this group in which all but 10 per cent. of the patients present more than one type of recognizable structural involvement. Such a state of affairs, wholly in keeping with the experience of the postmortem pathologist, holds out much encouragement to the clinical syphilographer, who finds that the efforts of his team are bringing to diagnosis in the living some of the accuracy and comprehensiveness that have so long been monopolized by the prosector for the dead.

IMPORTANCE OF RECORDS IN SYPHILOLOGY

The adequate record is a necessary accompaniment of the newer methods of diagnostic approach. All of us appreciate how much Fournier's encyclopedic knowledge depended on his records. My own enthusiasm on the matter comes, however, from a source nearer home, in the form of H. S. Plummer's mastery of the clinical problems of the thyroid and the conceptions of record which he has incorporated in the "Goiter Sheet" or record form for goiter cases in use in the Mayo Clinic. The record system which Plummer has devised endeavors to set before the examiner in a printed form a pigeon-holed filing case for the disease, into every compartment of which can be dropped either a negative or a positive observation, a measure of time or quantity, or a measure of intensity on a scale of ?, 0, 1, 2, 3, and 4. The examiner begins at the top of the sheet, and, without option or omission, goes through the printed form to the bottom. The data are so indexed by guide letters and numbers that a body of records can be transferred by ordinary clerical help to an abstract sheet which makes the study of clinical relations comparatively simple. Such a system of record, I am convinced, has a permanent investigative value immeasurably greater than the spontaneous or drift record, in which the examiner follows mental leads and cues to a diagnosis, the written or dictated page setting forth the story of his wanderings. The weaknesses of Plummer's method are largely inherent in the fallibilities, obstinacies, and lazinesses of human examiners, and in the forgetfulness of patients and the inaccuracies of their thoughts and statements. None the less, the advantages greatly outweigh the disadvantages, since the latter affect all forms of medical record alike. A system of record for syphilis will, I believe, be useless for scientific control unless it contains definite information in terms of time and quantity on the following five points:

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[6] Dreyer, G.: Investigations on the Normal Vital Capacity in Man and Its Relation to the Size of the Body, Lancet **2**:227, 1919.

1. Negative as well as positive findings.
2. The personal resistance of the patient to infection and evidence of individual peculiarities in the course of the disease.
3. Data from which to infer, on definite knowledge in regard to, the strain and peculiarities of the infecting organism.
4. The duration of the disease.
5. The type, duration, and intensity of treatment.

Lacking accurate data on these five points the most complete history of symptoms will be useless for basic investigation, because the fundamental facts regarding seed, soil, and treatment, on which alone a comprehensive study of the crop or outcome can be based, will be lacking. The nature of syphilis itself imposes limitations on such material which will make its accumulation slow. Moreover, such accumulation must await the development of a diagnostic and therapeutic machine which cannot be built up in a year or perhaps even in a decade. In four years of steady effort in this direction with generous facilities I have completed in tentative form only three of four necessary record forms required for this type of work. One of the most potent stimuli that has reached me is the appreciation of Fordyce's remarkable collection of data on the therapy of neurosyphilis. To place the diagnosis and the therapy of syphilis at large on a similar and perhaps even more advanced basis of exactitude appeals to me as a syphilologic ideal of the first magnitude. As one goes over inferior material, the tangible evidence of his own lack of foresight or lack of facilities, he realizes the vital significance of the unmentioned fact in accurate large scale deduction. One understands, too, how the honest substitution of "no data" for the tempting clinical inference or speculation, would leave more than one clinical reputation, his own among the number, puffing for breath. Is it too much to hope that in proportion as we succeed in substituting certainties for probabilities in record we shall build substantial foundations for the clinical syphilology of the future, and introduce into a field of confusion and impression some of the exactitudes and controlled conclusions of actuarial and mathematical science?

I am afraid that I have already exhausted your patience, and for that reason I merely express my willingness to demonstrate to any of you who may be interested the very crude beginnings of a system of record that I am hoping may give me, to some extent at least, the mastery of my own data. The problems that beset one in its development would afford material for another paper and would be much enriched by your suggestions. Before your good will vanishes let me ask you whether it would not be worth while, now or at some future date, provided it has not already been done, for so influential a body as the American Dermatological Association to undertake in behalf of the syphilographer of the future some constructive work on the problems of record in syphilis to which reference has been made? I cannot but believe that in this direction there is need for immediate action to pave the way for many significant future achievements in the revival of clinical syphilology.

SUMMARY

By way of summary, let me say that I have tried to voice my belief that the revival of clinical syphilology calls for a new type of syphilographer, synthetic rather than analytic in temperament, whose qualities as an inspirer of men, a cooperator, interpreter and coordinator, will outrank his merely technical expertness in the minutiae of syphilologic diagnosis. Such a syphilographer will direct in his field the efforts of a highly complex diagnostic organization rather than perform a few special tests. He will become expert in the appraisal of the relative significance of a variety of structural and functional investigations which he does not himself necessarily perform. He will endeavor to give concreteness to the intuitive and he will find in highly developed and systematized records that mastery of data which his synthetic powers require for the attainment of a new type of exactitude and conclusiveness in clinical research.

DISCUSSION

Dr. Corlett was much interested in Dr. Stokes' excellent paper and agreed with what he said. A long time ago he had maintained that dermatology and syphilis go hand in hand, and conceived of the ideal syphilographer as one sufficiently well equipped to handle all these cases, but at the time the ideal seemed impracticable. Many years ago, when the Lakeside Hospital was opened, the trustees decided not to have syphilitic patients in the hospital. Of course, this would have been an ideal situation, but they soon found syphilis among the orderlies and nurses, as well as in general medical and surgical cases in patients who came in for treatment of other ailments.

The board of managers thereupon recognized that syphilis had to be reckoned with, and they organized the Department of Skin Diseases and Syphilis. All cases of syphilis of the eye, nose or throat came through the skin department and were then referred to the different departments for special treatment. Most difficulty was experienced with the Department of Internal Medicine, the members of which have never worked with that hearty cooperation which the reader of the paper evidently enjoys. Cases of syphilis were then referred back to the Department of Dermatology and Syphilology for systematic treatment, and the patients were discharged by this department. In this way the necessity for these patients to come back in two or three years for further treatment or for treatment of a new outbreak was prevented. The organization was not such as that Dr. Stokes is fortunate to work with, but Dr. Corlett believed that this was the ideal organization, of value alike to the dermatologist and syphilographer.

Dr. Fordyce was much impressed with Dr. Stokes' excellent presentation of this subject. He felt that every one agreed in the proposition that Dr. Stokes had advanced; namely, that more attention should be paid to group medicine. Only in this way could the patient be placed under the best condition to receive the necessary medical attention. The syphilographer should also by such cooperation acquire a more comprehensive grasp of the disease. There are not many trained syphilographers in this country. Many know one phase of this subject but few have a broad knowledge of it in its entire aspect. In institutions organized on the lines of the Mayo Clinic opportunities are afforded the younger men to familiarize themselves with all phases of the disease. Men so trained will eventually exercise a profound impression as a whole. In the institution with which the speaker is connected cooperation is gradually being brought about between the departments of medicine, neurology, ophthalmology, obstetrics, etc. They have, however, not yet reached the stage of the frequent and instructive conferences referred to by Dr. Stokes chiefly because of the time occupied in teaching large classes of students and lack of opportunity for representatives of the various departments to get together.

The only point in Dr. Stokes' remarks that Dr. Fordyce criticized was his reference to the employment of an acute Wassermann system. Why not use an acute Wassermann system? The system employed by the Mayo Clinic might be sufficient but, according to Dr. Stokes, it was rather insensitive. In the early or florid stage of syphilis it is easy to obtain a positive Wassermann reaction with any of the systems used. In treated syphilis great difficulties are found. The cholesterin antigen may give a positive reaction in a certain number of cases while the alcoholic antigen with the ice box fixation may give a certain number of negative results with the same blood. On the other hand, a certain number of negative reactions may be obtained with the cholesterin antigen and with the alcoholic antigen positive reactions. In order, therefore, to detect all cases of syphilis it appeared necessary to the speaker to employ more than one system.

Dr. Schamberg believed that Dr. Stokes had brought a valuable message and that the Association was indebted to him for it. There is perhaps no other disease which is so susceptible to group study and so much benefited by it as syphilis, because, as is well known, there is probably no other disease in which there is such a wide invasion of the whole body as there is in syphilis by the *Spirochaeta pallida,* and such a liability to attack on all of the organs and viscera. He thought the members of the Association would agree with him that special emphasis should be placed on the point that there comes a time in the life of a syphilitic patient when treatment may be lessened in intensiveness or even suspended, even though we know he still suffers from syphilis; attention should be directed to determining the dominant resting place of the spirochetes, the organ or organs particularly attacked by the spirochete at the time—where the spirochete is doing damage. If the patient has a

+ + + + positive Wassermann reaction, treatment should not ordinarily be suspended. When dealing with a patient of 50, 55 years or older, in whom the roentgenograms indicate that there is no cardiovascular change of any importance and in whom spinal tests indicate that there is no neurosyphilis, he agreed with Dr. Pollitzer and others that it is not desirable to make any intensive effort to reverse the Wassermann reaction, and it might even be wise to suspend treatment. It is a question whether the treatment under such circumstances may not be more of a menace to the patient and the integrity of his organs than is the disease itself.

Dr. Schamberg believed the group study of syphilis to be particularly important when the spirochetes were inducing changes that were interfering with the capacity of certain organs. He thought another phase of the group study was that of congenital syphilis; he felt that the whole chapter of congenital syphilis would have to be rewritten. What has been recognized as congenital syphilis in the past have been the obvious stigmas, such as the Hutchinson teeth, disease of the joints and bones, keratitis, and so on. The profession must realize that children of syphilitic parents may be born in apparent good health and may later manifest abnormalities in the way of persistent anemia, loss of weight, or subtle tissue changes not ordinarily attributed to syphilis. The proof of the nature of these conditions is that only by syphilitic treatment may such patients be restored to health. He believed that tens of thousands of people throughout the country are suffering from anemias, vascular thickenings and other disturbances that are not attributed to the true underlying cause. In his clinic he has a pediatrician who is detailed to examine the children of syphilitic parents especially to determine whether or not they are affected in this manner.

Dr. Pollitzer said that aside from the pleasure he derived from listening to this paper, his principal emotion was one of envy. He could not help envying a man who was in a position to carry out the study of syphilis in the way in which Dr. Stokes had been able to do it. He had been very much interested in the group study of syphilis. It was about ten years since he had attempted to carry out something of this plan of treatment in an institution with which he was at that time connected. Unfortunately, there was not so much altruism, or so much scientific spirit in that institution as there is in the Mayo Clinic. The ophthalmologists, the surgeons, and the genito-urinary men were all afraid they might lose a patient if they sent him to the syphilographer, but he had advocated, in a small crude way, that which is being carried out at the Mayo Clinic. He had had better results in persuading the Department of Health of New York City which had actually made it a part of the sanitary code of the city that in any institution treating venereal diseases, syphilis should be treated in one department. Dr. Pollitzer emphasized the fact that this was a definite achievement and although, like many laws, it is rather inadequately carried out at present, the fact that it is on the statute book makes it a good thing and it is carried out in a good many institutions. Already in several institutions in New York every patient with syphilis is referred to the department of dermatology and syphilis. He believed the importance of this to the patient could not be sufficiently emphasized. The patient who goes to the ophthalmologist or the surgeon may be freed from his eye or bone lesions but his syphilis continues and no one is interested further in the asymptomatic syphilitic. From the standpoint of the patient, Dr. Pollitzer believed the work which is carried out at the Mayo Clinic is of the highest character.

Dr. Wile said that everything had been stated by those who had preceded him in appreciation of Dr. Stokes' paper. Dr. Stokes had made order at the Rochester clinic of what Dr. Mayo said was "syphilologic chaos" before he came.

Dr. Wile subscribed to Dr. Fordyce's and Dr. Schamberg's views regarding the Wassermann reaction. He believed that the present test, which was the last word at the moment, would more than likely be supplanted by a more delicate one in the future and that it therefore could not be too heavily leaned on at present. The thing which impressed him most and on which he would like to lay most emphasis was what he deemed the mistake of attempting to connect the Wassermann reaction with treatment. The exact biologic nature of the reaction was as yet unknown to any one. In view of this fact, persistent positives in the presence of intensive treatment were difficult to explain. In still other cases, in which the test was negative, it was still possible that the patient had syphilis. In view, therefore, of the doubtful status of the nature of the reaction, Dr. Wile felt that it could not be with accuracy relied on from the therapeutic standpoint.

Dr. Irvine was very much interested in Dr. Stokes' paper. In his opinion the part that should be particularly emphasized, for the need of the Association, was that the individual members should feel the importance of putting their work on such a basis, particularly those who were in teaching institutions. He doubted whether dermatologists felt the responsibility they should have in teaching syphilis. He was sure there were many schools that did not teach syphilis as it should be taught, and that their students are obtaining a wrong idea both as to the treatment of syphilis and syphilis itself. In trying to establish an organization, such as Dr. Stokes had suggested, they secured the cooperation of the many special departments by making it plain that they could continue to see and demonstrate their patients with syphilis of the eye, ear, etc., and that the department of dermatology and syphilis was interested only in carrying out the routine treatment of such cases and not in teaching syphilis of these various organs. With this understanding, all cases of syphilis are now referred to the department of dermatology and syphilis. Dr. Irvine thought the point Dr. Stokes made of treating group symptoms should be emphasized, as well as the need for the dermatologist to assume the responsibility of the teaching of the proper diagnosis and treatment of syphilis.

Dr. Pusey, while listening to the almost ideal conditions for treating syphilis which Dr. Stokes outlined, found himself paraphrasing an old negro song, "Earth is our abiding place, but Heaven is Stokes' home." When it came to the treatment of syphilis, Dr. Stokes' situation seemed to be one that the rest could only aspire to when they were translated. He thought that Dr. Stokes' outline was interesting and useful in the suggestions which it gave of the value which dermatologists and the profession generally, might obtain from more cooperation in the treatment of syphilis.

Dr. Stokes (closing) said one or two points were brought out in the discussion which he wished to take up. First, Dr. Fordyce mentioned using a more acute Wassermann test. He would have explained his sympathy with that idea if he had not felt so hurried. He felt that while the acute Wassermann is best, it is hard for the specialist to realize the crutch which the Wassermann test is to the general man, and that it is really an advantage to be able to say to him as a means of encouraging clinical judgment that only 40 or 50 per cent. of his cases would be positive in the presence of syphilis rather than 100 per cent. Dr. Sanford and Dr. Stokes were considering the introduction of a more sensitive Wassermann test, which they hoped would identify more latent cases. He had mentioned in his paper on railroad men that a Wassermann test taken between the ages of 17 and 31 would probably get most of the asymptomatic positive Wassermann results that it is possible to obtain.

One of the most interesting studies he had recently undertaken was that of Wassermann positive syphilis which remains persistently positive after long continued treatment. He had found that only 10 per cent. of the cases studied had Wassermann-positiveness as the only evidence of the disease. Involvement of the cardiovascular system was recognized by a sufficiently intensive study as the commonest manifestation of the disease. It was particularly interesting to see how the multiplicity of involvements, the polytropism of the disease emphasized by postmortem findings, could be identified clinically by multiple diagnostic attack.

The matter of record was growing to be one of increased importance in the study and treatment of syphilis. It appeared to him that the Association would be taking a step in the right direction by organizing a committee to consider the subject of record in syphilis and its improvement.

REINFECTION AND CURABILITY IN SYPHILIS

LEO JACOBI, M.D.
NEW YORK

Reports of reinfection in syphilis have been appearing with increasing frequency during the past year or two. The presentation of such a case before a meeting of dermatologists is certain to precipitate a lively and somewhat acrimonious discussion, which, after ranging far afield, usually ends in an impassé. In the confusion of debated issues, however, a sharp cleavage of opinion becomes clearly discernible: one group, which may be called the conservative, holds fast to orthodox views, while the other, less imbued with respect for authority, appears hospitably inclined toward new conceptions. It may be interesting, and perhaps helpful in clarifying our ideas, to analyze in detail the arguments and the method of reasoning employed by the disputants.

As a rule, the validity of reinfection is vigorously contested by skeptics of the old school, strong in the conviction that syphilis, having once invaded the human body, becomes a permanent possession, and can never be shaken off. Their mode of reasoning, reduced to its simplest terms, assumes the form of the following syllogism:

1. Reinfection is impossible in uncured syphilis.
2. Syphilis is an incurable disease.
3. Therefore, reinfection is impossible in syphilis.

Intrenched behind this deduction, they say to their opponents: first prove that syphilis can be cured, and, until you have done so, cease prating about reinfection. To this challenge the progressives reply by a complete reversal of minor premise and conclusion. Granted, they retort, that reinfection can take place only after syphilis has been cured; but reinfection does occur in syphilis, as our cases show: therefore, syphilis is a curable disease.

CURABILITY AND REINFECTION

The antagonism appears to be irreconcilable. Prove that syphilis can be cured and we shall then accept your cases of reinfection, says one side; accept our cases of reinfection and we shall then have proved that syphilis is curable, is the rejoinder of the other.

Yet, in spite of reversed premises and conclusions, both are found tacitly acknowledging the intimate connection between curability and reinfection. Both accept the contingency of the latter on the former as an article of faith.

And it is here, precisely in this reluctance to divorce the two conceptions, that we must look for the real obstacle to a mutual understanding. Strange as it may seem, unanimity on this point is the subtle cause of the entire controversy, and if it could be shown that reinfection is not necessarily contingent on curability, discord would promptly give place to harmony.

It is therefore necessary to submit the proposition: "reinfection cannot take place in uncured syphilis," to a searching analysis, even though it may seem dangerous heresy to doubt a statement so long regarded as almost axiomatic.

Expressed in clear and concrete terms, the proposition in question means that the presence of the *Spirochaeta pallida* (or its transitional forms) in the human body renders the latter unconditionally and absolutely immune against a new invasion by the *Spirochaeta pallida*. Confronted by a thesis so startling and categorical, one naturally expects to find it fortified by every possible proof, and placed beyond the reach of doubt or criticism. As a matter of fact, however, a closer examination of the evidence fails to substantiate such an expectation, and even emboldens one to put the following query: When, where, and by whom has it been indisputably proved that the *Spirochaeta pallida* or its transitional forms must be completely eradicated from the system, before a new invasion by the *Spirochaeta pallida* can occur?

Having squarely faced the issue, we are soon compelled to admit that this "law" derives its alleged validity mainly from assertions made by the great authorities of the past and handed down to us by tradition, assertions which, despite their venerable age, cannot usurp the place of logical argument. In fact, it is difficult to see how adequate proof could have been adduced during the clinical era of syphilology, before the discovery of the *Spirochaeta pallida,* when the only criterion of cure was the absence of clinical manifestations. In our own time, made a little less ignorant by the spirochete and by the Wassermann test, syphilographers nevertheless also have failed to prove that reinfection cannot occur unless syphilis has been cured, or, in other words, that the presence of the parasite renders the host absolutely immune.

The truth or falsity of this allegation could be demonstrated by rigidly conducted experimental inoculations with the *Spirochaeta pallida,* made on persons known to be harboring the parasite.

If long series of such inoculations, carried out under scientific conditions in various stages of the disease, and with various strains of the *Spirochaeta pallida,* were to produce unequivocal results, then, and only then, could we take a definite stand in the controversy. Have such experiments been made on an adequate scale? The answer can hardly remain in doubt. To be sure, it has been found that autoinoculation with the virus of the hard chancre is successful during the first week or two, but this knowledge has little value, beyond indicating the approximate time when immunity becomes established. Again, during the the florid period of syphilis, when the system is flooded with parasites, the existence of a strong immunity need scarcely be questioned, though even here inoculations with different strains of *Spirochaeta pallida* might be productive of interesting results.

But it is in the later stages of syphilis, after the conflagration has been reduced to smoldering embers, that we may expect to find a gradual weakening of immunity, and a corresponding susceptibility to a new inoculation. It would be most interesting and instructive, for example, to inoculate cases of general paresis with the specific virus. In this disease, living spirochetes have been found in the brain tissues, but it is quite conceivable that they no longer confer an immunity sufficiently strong to resist a new invasion through the skin or mucous membranes.

Of course, the practical difficulties in the path of such researches on the human subject are well-nigh insurmountable, and we are reduced to the necessity of waiting until the patient takes the matter out of our hands and makes a successful test on his own account. Still, there is an alternative, and that is animal experimentation. Recent studies on animals make the existence of different strains of *Spirochaeta pallida* highly probable, and attempts have been made to classify them, distinguishing a dermotropic variety from a neurotropic, the former showing an affinity for the skin and causing the cutaneous manifestations of syphilis, while the latter, by its selective action on the central nervous system, induces paresis and locomotor ataxia.

Furthermore, it has been found that animals experimentally infected with one variety may be successfully inoculated with the other, developing a new primary chancre. Thus the belief is already beginning to emerge that a new invasion by the *Spirochaeta pallida* is sometimes possible before the old has been completely extirpated. Perhaps the term "superinfection" would be more acceptable to purists when referring to these cases, though reinfection can be defended on etymologic grounds.

Side by side with these results of animal experiments, we encounter in recent literature occasional mention of an attenuated immunity that might make reinoculation successful in the human patient. Thus, while much work remains to be done before the final verdict can be pronounced, it is already becoming more and more evident that the ancient ties that bound together the conceptions of curability and reinfection have at last been effectually loosened, if not entirely severed.

Reinfection is a question of immunity, not of cure. In the future book on immunity, syphilis will be found to occupy a chapter, and reinfection a paragraph. Theoretically, it is quite conceivable that the patient may be cured, that is, completely purged of the *Spirochaeta pallida* or its transitional forms, and yet left in the possession of an absolute and life-long immunity, which would imply the impossibility of reinfection. On the other hand, syphilis might be conceived as an incurable disease, conferring an immunity that gradually declines as the date of the primary infection recedes, until a point is reached at which a fresh inoculation may be successful.

Bearing all this in mind, it will be advantageous henceforth to dissociate the two conceptions of curability and reinfection, and to consider them as separate problems. The answer to the one need not of itself furnish a solution to the other, but each will require its own structure of logical proof.

The first question, that of curability in syphilis, will have to be settled on the strength of clinical, serologic and pathologic evidence. The old syphilographers had to depend almost exclusively on clinical observation. Impressed by the treacherous and protean manifestations of late syphilis, occurring long after infection even in well-treated cases, these authorities show a distinct leaning toward a pessimistic view. Their unfavorable clinical experience hardened into a settled belief that "once a syphilitic, always a syphilitic," and this conception has been transmitted to many of their modern descendants, who consider syphilis an ineradicable disease. In addition to clinical evidence, they can point to such pathologic findings as those of Warthin, who in postmortem examinations demonstrated the presence of living spirochetes in the tissues taken from syphilitic persons who were apparently cured, i. e., gave neither clinical nor serologic evidence of syphilis.

This discovery emphasizes the extraordinary difficulties confronting those who cherish the belief that syphilis is curable and seek for something more tangible in the way of proof than mere conjecture. Indeed, how can one obtain the assurance that a given patient no longer harbors the *Spirochaeta pallida?* Since no reliance can be placed on the absence of clinical phenomena, and since the Wassermann test is not sufficiently delicate and trustworthy, we are left without an absolute criterion of cure and reduced to waiting until future research shall have supplied us with an infallible method of detecting the presence of the *Spirochaeta pallida* in the human body. In the meantime, believers in curability are at the mercy of pessimists, who, refusing to surrender the old dogma of incurability, shift the burden of proof to the side of the optimists.

It is precisely this feeling of helplessness that drives the latter to offer their cases of reinfection as proof of curability—an entirely illogical proceeding, as we have seen. Reinfection does not imply the absence of living spirochetes in the host, but only indicates that the immunity left in the wake of the preceding attack has lost some or all of its original virtue.

Thus the question "Is syphilis curable?" will have to be relegated to the innumerable other problems awaiting future revelations. This is unfortunate, as it deprives the patient of a much-needed solace, and, moreover, leaves the field to the pessimist, who adds to the actual terrors of the disease those of despondency and mental distress.

PRESENT STATUS OF REINFECTION IN SYPHILIS

Let us turn now to the present status of the vexing problem of reinfection in syphilis. Here we find ourselves treading firmer ground. Having emancipated our mind from the old dogma which made reinfection dependent on curability, we are enabled to take an unbiased view of the evidence presented in favor of reinfection. In judging a given case, more weight should be placed on the clinical phenomena than on the intricacies of dialectics and the uncertainties of repeated Wassermann tests. If a patient who had once been infected with syphilis comes to us with a suspicious lesion on the genitals appearing several days or weeks after exposure to infection; if the related inguinal glands become enlarged, hard and painless; if, in due time, secondary manifestations make their appearance, what diagnosis, other than a new syphilitic infection, can be made, even without the finding of the spirochete and a positive Wassermann reaction?

If, in addition, the *Spirochaeta pallida* has been found in the initial lesion, and if, furthermore, the Wassermann reaction, having been negative before the appearance of the new chancre and for some time afterward, now turns to positive, the evidence in favor of reinfection becomes so overwhelming that only one steeped in prejudice and sophistry will remain unconverted.

Caution is necessary in accepting the patient's statement that he has already been the victim of syphilis, and in differentiating the new initial lesion from chancre redux or a gumma; but these and other similar sources of error can usually be eliminated.

It is at this juncture that we again meet the pessimist, who, driven to the wall, takes refuge in the ancient legend, "Once syphilis—always syphilis," and closes his eyes to facts.

It then becomes our duty to inform him that he is laboring under a false conception, or else that he belongs to the category of those perverse persons who have been characterized nineteen centuries ago as having eyes yet seeing not.

The majority of open minded observers have by this time taken their stand in the controversy, and I am on the side of those who regard reinfection as definitely proved.

SUMMARY

In conclusion, our analysis may be summarized as follows:

1. The question, "Is syphilis curable?" cannot be answered definitely in the light of our present knowledge.

2. The occurrence of reinfection in syphilis may be accepted as an established fact.

3. Reinfection, however, is by no means evidence of curability.

These two conceptions do not stand and fall together, as many believe; they are not contingent on each other, and should be dissociated in the interest of clear thinking and unbiased judgment.

EXPERIENCE WITH SODIUM DIARSENOL

PRELIMINARY NOTE

FRANKLIN R. WRIGHT, M.D., AND HENRY E. MICHELSON, M.D.
MINNEAPOLIS

We have used ten tubes of sodium diarsenol furnished by the Diarsenol Company of Buffalo and thought that this preliminary note might be of service to others who wish to use this product. The drug was used in four cases.

REPORT OF CASES

Case 1 (No. 261).—A man, aged 36, single, presented himself on June 8, 1920, with four small indurated papules on the corona and an ulceration at the frenulum. *Spirochetae pallidae* were easily demonstrated. The Wassermann reaction was negative. On June 8 he was given 0.45 gm. of sodium diarsenol; on the 9th he received 0.6 gm. and on the 10th he again received 0.6 gm., that is, he received three doses on each of three successive days. He had no reaction and the therapeutic effect was equal to that of any preparation we have used. On June 14 he reported for mercury treatments and the papules were entirely healed.

Case 2.—A man, aged 30, presented himself on June 8, 1920, with an ulcer the size of a nickle on the mucous membrane surface of the prepuce. The inguinal lymph nodes were enlarged, *Spirochetae pallidae* were easily demonstrated and the Wassermann reaction was negative. On June 8 he received 0.45 gm. of sodium diarsenol and on the 9th he received 0.6 gm. In the evening he suffered with severe nausea and vomiting. This may have been due to the fact that he disobeyed orders and ate a rather heavy meal. The dose was not repeated until June 11 when he again received 0.6 gm.; this time there was no reaction. He reported again on June 15. The ulcer was diminished to one third its original size. Again the therapeutic effect was all that could be expected.

Case 3.—A man, aged 23, presented himself on June 15, 1920, with two indurated ulcers, one on the glans and the other on the opposing mucous membrane surface of the prepuce. *Spirochetae pallidae* were easily demonstrated. The Wassermann reaction was positive. Pallor and general malaise were marked and the inguinal lymph nodes were much enlarged. On June 15 he was given 0.45 gm. of sodium diarsenol. He complained that after four hours he was seized with a severe chill and severe depression. He felt somewhat dizzy but had completely recovered on the following afternoon. On the next day the lesions were distinctly flattened. On June 17 he received 0.6 gm. without any particular reaction.

Case 4.—A young man, aged 19, presented himself on June 8, 1920, with a small eroded papule on the glans. *Spirochetae pallidae* were present. He received that evening 0.6 gm. of neosalvarsan (Metz). He did not report again until June 11, when the lesion was one-half its presenting size. He then received 0.6 gm. of sodium diarsenol and was not seen again until June 15. The lesion was then completely healed and he had not had any particular reaction with the last injection. All of the injections were in 20 c.c. of sterile distilled water.

We contemplate using 500 tubes in the university clinic and hope to publish detailed reports later.

THE ACTION OF RADIUM ON A VARIETY OF CUTANEOUS CONDITIONS

DOUGLASS W. MONTGOMERY, M.D.
AND
GEORGE D. CULVER, M.D.
SAN FRANCISCO

The use of radium in cancer, whether for amelioration of the symptoms or cure of the disease, is so beneficent that it has overshadowed its use in a great number of other affections. In the conditions discussed it has afforded us valuable service.

PERSISTENT FISSURES OF THE NARES AND LIPS

As the result of catarrh, cracks may form in the nares, especially frequently in the anterior angle. These are often associated with folliculitis of the vibrissae. The usual infective agent is a streptococcus, and it often gives rise to localized attacks of erysipelas, and after a time, to permanent redness of the nose. In fact, it is one of the principal causes of red nose. The best routine treatment is the use of boric acid fomentations, and the employment of a 12 per cent. calomel ointment, under which almost all cases will clear up. Some cases, however, are refractory.

A man, 37 years of age, had been under the care of a competent physician for this condition in the left nostril for one year before coming to us. The refractoriness in this case may have been due to inflammatory induration and to streptococci lying latent deep in this induration, as they are now known to do. We were confronted by an unusually stubborn case, and in addition to the boric acid fomentations and the calomel ointment, we employed radium.

On July 21, two 25 mg. tubes, screened with a silver tube of 0.35 mm. wall thickness and a rubber cot, were placed in the left nostril for fifteen minutes. By August 22 the condition was much improved, but there was still a little sensitiveness at the tip of the anterior angle. An 11 mg. radium plaque, shielded with a rubber cot, was placed over this region for five minutes. By September 15, the man had completely recovered, and we have heard of no relapse.

In this case it might be objected that radium with 0.35 mm. silver screening for fifteen minutes would have no effect—that the screening was too heavy and the time too short. This tube, however, was itself highly radioactive as the radium was constantly kept in it.

Another instance of fissuring occurred in a soft, pulpy man of 49, weighing 205 pounds, who had been troubled with the nasal condition for the previous three months. He was also afflicted with cracking and irritation of the perineum and anus. After a preliminary treatment which proved ineffectual, radium was used in both situations. The relief was prompt; the anal discomfort disappeared within twenty-four hours.

LUPUS ERYTHEMATOSUS

To us one of the chief inducements for using radium was its favorable effect on that stubborn affection, lupus erythematosus. Its effect is greater than could be expected, for the eruption of lupus erythematosus is only a symptom and the real origin of this symptom lies in some hitherto not demonstrated internal affection.

We have found that the best results are obtained with very slight screening, and after an application of long duration. We employ a standard sized plaque which contains 11 mg. instead of 10 mg. of radium element, with a screen of two thicknesses of writing paper, for thirty minutes. Distance must always be considered an especially excellent screen, and distance is often secured by interposing cellulose, such as paper or felt. In lupus erythematosis, however, too great a distance is not desirable. A patient, an intelligent young man, deeply interested in his trouble and in the effect of radium on it, noted that the areas treated with the plaque in quite close contact with the affected surface, only screened with two thicknesses of writing paper, produced better results than when a thicker screen was interposed. A lead shield placed about the patch also interfered with obtaining the best results. Apparently close contact and wide inclusion of the margins, so as to radiate well beyond the visible border, is desirable.

DYSTROPHY OF THE NAILS IN SEBORRHEIC ECZEMA AND PSORIASIS

Sometimes in the disease above mentioned, the deformities of the nails are the most distressing lesions, as in the case of a dentist who thought he would have to change his occupation because his nails were so ugly and so difficult to clean.

On Sept. 27, 1919, a woman consulted us concerning dystrophy of the nails. The trouble had begun one year before as a redness and crusting in the nail fold. The fourth and fifth fingernails of the right hand and the fourth finger of the left hand were affected. Besides this, she had seborrheic eczema of the nasolabial folds, patches of psoriasis on the right elbow tip and on the right leg just above the external maleolus.

Any one acquainted with the obduracy of these cases of seborrheic paronychia before the introduction of the roentgen-ray or radium will appreciate the results we have obtained through these mediums. In addition to general treatment, we employed lightly screened radium plaques over the nails for short periods of time. After a fairly strong reaction, the nails grew out normally.

LICHEN HYPERTROPHICUS

The eruption of lichen planus is usually so widespread that roentgen-rays are much more easily utilized than radium, but recently we had a case of "white spot" disease with two hypertrophic lichen papules on the back of the neck. These papules were each 11 mm. long and 6 mm. broad. They were raised, oval, with a pale, rather milky colored border, and a rough center studded with follicular openings filled with small, horny comedos. There were pale, milky bands running across the top of the papules between the follicular openings. Radium, lightly screened, acted well on these papules, and caused their disappearance. We doubt whether roentgen rays would have acted as well.

VENEREAL WARTS

A man, 21 years of age, while under treatment for syphilis, developed papillomas in the anterior part of the urethra. A 25 mg. tube of radium, enclosed in its silver capsule, 0.35 mm. wall thickness, and covered with one thickness of writing paper and one thickness of zinc oxid adhesive plaster, was inserted and kept in place for forty-five minutes. This was done April 8, 1919, and by April 24 the papillomas were disappearing rapidly. In a short time they cleared up entirely, leaving no trace.

PATCHES OF INDURATED ECZEMA

There are patches of indurated eczema in which the induration and the pruritus are the main clinical features. These may be limited in extent, and as refractory to treatment as they are limited. The following case is a good example of this annoying affection.

A woman, 64 years of age, suffering from aortic regurgitation with marked pulsation in the neck, an enlarged liver, and sluggishness of the bowels, consulted us on account of a lump on the inner surface of the right natis. It was red, raised, rounded, sharply bounded, but was evidently eczematous and not neoplastic in its nature. It was not a keloid. We were able to reassure the patient in regard to tumor formation, but the prognosis as regards the cure of these cases is anything but good. As these patches are very itchy, the outlook is not cheerful. We were, however, able to control entirely the pruritus with salicylic acid plaster mull (5 per cent. strength). The thickening remained, however, and two or three days after discontinuing the use of plaster the pruritus would return. By April 27, 1917, the affection had improved, but there was still a small edematous, red patch left, which we knew would rapidly assume its original dimensions and irritability on removal of the salicylic acid plaster. We were frankly discouraged as far as the hope of achieving a permanent cure was concerned.

We were preparing the patient for a life-long use of this remedy when we fortunately employed radium. On April 27, 1917, after eighteen months of other treatment, a radium plaque containing 11 mg. of radium element was placed on the patch, shielded with one thickness of writing paper and one of rubber tissue, and retained ten minutes. This completely relieved the itching, and there was no trace of the induration on June 12, 1917. To make sure, however, we again used this same plaque for ten minutes, screened with 0.50 mg. of aluminum. There has been no return of the condition since that time.

COMMENT

These few cases give some idea of the wide application of this remedial agent in diseases of the cutaneous envelope. The ease of its application, its painlessness and its excellent results make it one of the most valuable additions to the dermatologist's list of effective remedies.

Correspondence

"THE EFFECT OF MERCURY SALICYLATE ON THE WASSERMANN REACTION"

To the Editor:—I have read with much interest Dr. Herman Goodman's article on "The Effect of Mercury Salicylate on the Wassermann Reaction," in the August number of the *Archives of Dermatology and Syphilology.* I thought all syphilologists were past that milepost of knowledge which marks the use of liquid petrolatum as a vehicle for intramuscular injections. It has repeatedly been shown that the material is not absorbed, and that about all the physician gets is a paraffinoma for his pains.

I think Dr. Goodman also erred in the matter of dosage. Few of us would expect to secure permanently beneficial results following one grain doses of mercury salicylate, injected at intervals of one week, even if an absorbable medium were used.

I have been employing mercury salicylate, in an olive oil and lanolin emulsion, for more than twelve years, and while I occasionally branch off and try some other highly recommended preparation, I have invariably returned to the old standby, for I am convinced that when properly employed it is one of our most potent and reliable remedies in combating syphilis.

Richard L. Sutton, M.D., Kansas City, Mo.

"THE EFFECT OF MERCURY SALICYLATE ON THE WASSERMANN REACTION"

To the Editor:—Although Dr. Sutton may very properly criticize the method of using mercury salicylate described in my article, "The Effect of Mercury Salicylate on the Wassermann Reaction," on the ground that, in his opinion, the dosage and vehicle are objectional, it is hardly accurate to suggest that the method is antiquated and not in use by modern syphilographers.

As to the vehicle: Liquid petrolatum is a menstruum which has been and is being largely used. Stellwagon, Hazen, Ormsby—to take the first illustrations that come to hand—all give liquid petrolatum or its equivalents as a vehicle for mercury salicylate. The "Army Manual of Treatment of Venereal Diseases" gives the same menstruum, as does the Public Health Service edition of that manual.

As to dosage: Perhaps no one in this country or elsewhere has given so much attention to the safe dosage of mercury as have Schamberg and his coexperimenters of the staff of the Dermatological Research Laboratories. In a pamphlet on the treatment of syphilis just issued from these laboratories the following statement on this subject appears: " . . . the insoluble compounds, if used at all, should be limited to one grain doses . . ." Elsewhere the same authors say: ". . . A word of caution must be sounded for the insoluble mercurials; administered as they usually are, once a week, they are sure to accumulate in the body . . ."

Herman Goodman, M.D., New York.

Abstracts from Current Literature

THE STRUCTURE OF NORMAL FIBERS OF PURKINJE IN THE ADULT HUMAN HEART AND THEIR PATHOLOGICAL ALTERATION IN SYPHILITIC MYOCARDITIS. O. Van Der Stricht and T. Wingate Todd, Johns Hopkins Hosp. Rep. **19**:1, 1920.

This monograph, of considerable interest to the worker in the pathologic anatomy of syphilis, presents the following points which relate to the changes in the structure of the fibers of Purkinje produced by syphilis. Longitudinal cleavage of Purkinje cells is manifested in the normal heart, but in the syphilitic organ this condition is so marked that it must be considered pathologic. Because of the hypertrophy of the interstitial connective tissue the cleavage affects a much greater number of Purkinje cells and constitutes the most important factor in the atrophy and disappearance of many of these elements. In the pathologic heart the connective tissue septum (endomysium) of cleavage can undergo a considerable thickening and invade the neighboring daughter cells in its turn, subdividing them into smaller symmetric or asymmetric elements, the diameter of which hardly surpasses that of a smooth muscle cell. These markedly atrophied cells still possess, when they have retained the features of Purkinje type, a myofibrillar cortical layer and an axial sarcoplasmic zone between which there often appears an internal cytoplasmic membrane.

The atrophied elements in their turn may undergo cleavage into smaller fragments which may be nucleated or devoid of nuclei. The latter type represents the last vestiges of the Purkinje cell before its disappearance or complete sclerosis. The pathologic cleavage of the Purkinje cell may be accompanied by amitotic division of the nucleus induced by the extension of the endomysial septum. In certain cases blood capillaries seem to play a predominant rôle in the invasion by the endomysium. Purkinje cells present a special morphology in accordance with the special functions which they fulfill. They possess the power of evolving and of transforming themselves into cardiac elements even in the normal state, but in the pathologic condition this process of transformation may become so accentuated that it appears as possibly constituting an important factor in the production of derangements of cardiac rhythm. Surrounding the Purkinje cells laterally there is a very thin endomysial membrane continuous with the cleavage partitions appearing in the division of a mother cell. It should be considered as a production not of the peripheral cytoplasm of the muscular cell but of the neighboring endomysium. It corresponds then to a kind of false sarcolemma. In the pathologic condition this sarcolemma may undergo considerable hypertrophy and with the sclerosed interstitial connective-tissue it forms a second very important factor which in the process of cleavage may exercise a marked influence toward the atrophy of the Purkinje elements.

The endocardium which covers the different segments of the atrioventricular bundle is of variable thickness. In the normal heart it is notably thicker in the right atrium than in the ventricles and it is thicker in the left ventricle than in the right. In the syphilitic heart it undergoes considerable hypertrophy in the ventricular areas especially in the left ventricle. It therefore participates in the sclerotic process which affects the atrioventricular bundle. Elastic fibers are very abundant in this endocardium and in certain locations they produce three successive networks which tend to become transformed into fenestrated elastic membranes. The increase in diameter of the pathologic endocardium is due not only to the formation of new collagenous bundles, but also to the production of numerous elastic elements. The endocardium related to the different segments of the atrioventricular bundle may include isolated scattered smooth muscular fibers, isolated bundles or sometimes more or less continuous layers of smooth muscle fibers. In the normal heart these are much more numerous in the atrium than in the two ventricles and a little more numerous in the left ventricle than in the right. In the syphilitic heart they are markedly diminished in number in the two ventricles and even in the atrium. There seems no doubt that the sclerotic process has exercised a considerable influence toward their reduction in number.

In the pathologic heart there exist traces of a slight diffuse inflammation along the majority of the segments of the atrioventricular bundle and its superficial endocardium. At certain levels in the left ventricle are to be observed centers of much more marked infiltration.

Sclerotic lesions of the interstitial connective tissue and of the small arterial branches, atrophy of the Purkinje fibers and diffuse inflammation are much more accentuated in the ventricles than in the atrium and particularly in the left ventricle.

Senear, Chicago.

SPECIFIC AORTITIS. W. D. Reid, Boston M. & S. J. **183**:67 (July 15) 1920; **183**:105 (July 22) 1920.

The author makes an exhaustive study of the subject and appends an excellent bibliography. He devotes considerable space to the pathology of the condition, both from a study of fifty-four necropsies at the Massachusetts General Hospital since the spirochetes in aortic tissue were demonstrated there for the first time in this country in 1909, and from a study of the literature.

This disease was present in 3.5 per cent. of the total number of necropsies at this hospital. The author's clinical material is derived from a study of the records of 105 patients treated for the disease at the same hospital. His conclusions are somewhat as follows: Syphilitic disease of the aorta is one of the most common and most serious findings in all cases of acquired syphilis. The lesion is essentially a mesortitis beginning first about the vasa vasorum and is a manifestation of active syphilitic disease, the spirochetes having been demonstrated in the lesion in eleven of his cases. The aortic process frequently extends to the aortic cusps and it has been shown that relatively often there is accompanying myocarditis of spirochetal origin. Aortic roughening and regurgitation, dilatation or aneurysm of the aortic arch and angina pectoris are common in syphilitic aortitis. Nonsyphilitic forms of aortitis are rare.

He discusses the subjective symptoms, shortness of breath, substernal pain, cough, and palpitation and takes up the physical signs under the subdivisions of inspection, palpation, auscultation, Wassermann reaction and roentgen-ray examination. Many cases may be called latent because symptoms are absent. Such cases are commonly undiagnosed until disclosed perhaps in a routine roentgen-ray examination. There is no one point on which diagnosis should be based, but only after a study of all the facts in a given case should a decision be rendered. Every case of cardiac disturbance of obscure origin, especially if the patient is a young adult and if there are signs of involvement of the aortic valve, should immediately suggest the possibility of syphilitic causation. A positive Wassermann reaction is of confirmatory value but is frequently absent. Roentgen examination, though unreliable in early cases, gives perhaps the most reliable findings. Syphilitic aortitis evidences a tendency to progressive impairment of the heart and aorta and is therefore of serious import. Treatment should be directed primarily toward killing the spirochetes in the aortic lesions. The use of both mercury and arsphenamin is advocated. Decompensation of the heart is to be treated as in that of nonsyphilitic origin.

The need for early diagnosis is emphasized, as well as the fact that there should be a greater willingness on the part of clinicians to make a tentative diagnosis and resort to a therapeutic test. Along such lines lies the greatest hope for improvement in the mortality rate of this disease.

Lane, Boston.

UEBER DIE SACHS-GEORGISCHE AUSFLOCKUNGSREAKTION (THE SACHS-GEORGI PRECIPITATION REACTION). Leo Kumer, Wien. klin. Wchnschr. **33**:562, 1920.

Although the technic of the Sachs-Georgi precipitation test for syphilis is apparently simple enough, it requires some skill and practice. In addition, not every antigen prepared serves the purpose; in one series only one of three extracts prepared similarly gave the reaction. The method of diluting the antigen is still under study, and one cannot say at this time whether rapid or slow dilution will give the proper test.

Clinically, the reaction has been reported for over 30,000 trials. In few cases of florid secondary syphilis has the reaction failed to be positive. Several nonspecific cases have, on the other hand, been reported as giving positive results. A modification in the hours of incubation is claimed to nullify this objection. Kumer has performed over 2,200 Sachs-Georgi tests, paralleling them with the Wassermann reaction. Eighty-one per cent. gave identical results, and if those with minor differences were included, the percentage of equivalent results reached ninety-one. In his first series of 1,245 cases, there were fifty-five spinal fluids: forty-eight gave negative Wassermann and Sachs-Georgi reactions; two gave positive Wassermann reactions and negative Sachs-Georgi reactions, and five gave negative Sachs-Georgi reactions and weakly positive Wassermann reactions. Study of the history and clinical examination showed that the Wassermann reaction persisted longer than the Sachs-Georgi. The assertion has been made that the Sachs-Georgi reaction precedes the Wassermann in primary syphilis. The authors had forty-four initial lesions; in five there was an agreement as to strongly positive, in six an agreement as to weakly positive, in twenty-one an agreement as to negative. In one case a positive Sachs-Georgi reaction paralleled a negative Wassermann reaction; seven patients with negative Sachs-Georgi reactions gave positive Wassermann reactions; and in three cases the differences were not marked.

The Sachs-Georgi is a valuable reaction; it cannot as yet be substituted for the Wassermann reaction, but is the most desirable test to parallel the Wassermann.

Goodman, New York.

A COMPARATIVE STUDY OF THE TRYPANOCIDAL ACTIVITY OF ARSPHENAMIN AND NEOARSPHENAMIN. J. F. Schamberg, J. A. Kolmer and G. W. Raiziss, Am. J. Med. Sc. **160**:25 (July) 1920.

The authors utilized rats infected with a virulent strain of *T. equiperdum* to determine the smallest amount of the drugs in question necessary to sterilize the animals inoculated with an approximately known number of organisms. The rats were inoculated twenty-four hours before medication was commenced, using doses of arsphenamin varying from 0.005 to 0.02 gm. per kilogram of rat and neoarsphenamin in doses of 0.008 to 0.04 gm.

The average minimal sterilizing dose of twenty-one compounds of arsphenamin from six different laboratories was found to be 0.023 gm. per kilo of rat while the average for neo-arsphenamin under the same conditions was 0.04 gm. per kilo of rat. The trypanocidal activity of the various compounds was found to vary in the same manner as the toxicity.

According to the results of these experiments, 0.6 gm. of arsphenamin equals 1.05 gm. of neo-arsphenamin in therapeutic activity, and the authors consider 1 gm. of neo-arsphenamin to have a greater margin of safety than 0.6 gm. of arsphenamin although arsphenamin has a trypanocidal activity which is 1.74 times greater than neo-arsphenamin.

Jamieson, Detroit.

COMPARATIVE STUDIES OF THE TOXICITY OF ARSPHENAMIN AND NEO-ARSPHENAMIN. J. F. Schamberg, J. A. Kolmer and G. W. Raiziss, Am. J. M. Sc. **160**:188 (Aug.) 1920.

Although the "lethal toxicity" of the drugs in question can be determined by experiments with rats and mice, these animals do not show any of the effects of the so-called "nitritoid crises" in man, the latter being due to some factor either in preparation or to the unidentified toxic substance "X."

These experiments show that arsphenamin injected intravenously by the method described can be tolerated by rats in amounts of 0.105 gm. per kilo of body weight which is equivalent in man to twelve times the usual maximum dose of 0.6 gm. By similar comparison with neoarsphenamin the rat toleration is 0.18 to 0.3 gm. or the equivalent of nineteen times the maximum (0.9 gm.) usually employed.

Subcutaneously arsphenamin is tolerated in rats in larger doses than neo-arsphenamin, in the proportion of 0.342 gm. to 0.177 gm. of the latter. This proportion is reversed when mice are used.

The authors conclude that the margin of safety is considerably in favor of neo-arsphenamin in the treatment of syphilis.

Jamieson, Detroit.

THE SIGNIFICANCE OF SYPHILIS IN PRENATAL CARE AND IN THE CAUSATION OF FETAL DEATH. J. Whitridge Williams, Bull. Johns Hopkins Hosp. **31**:141 (May) 1920.

A study of 302 fetal deaths occurring in 4,000 consecutive deliveries in the Johns Hopkins Hospital, including deaths during the last ten or twelve weeks of pregnancy and the two weeks immediately following delivery, revealed that syphilis was responsible for 34.44 per cent. of the entire number and that it caused more deaths than any other single factor. Of the 302 deaths, ninety-nine occurred in white and 203 in black infants, an incidence of 5.4 and 9.4 per cent., respectively. Syphilis was noted in 104 cases, in eighty-nine the diagnosis was confirmed by necropsy with the demonstration of spirochetes in the fetal tissues, while in the remaining fifteen it was based on clinical findings in the child, or on the presence of syphilitic lesions in the placenta associated with a positive maternal Wassermann reaction. Syphilis was the cause of 12.12 per cent. of fetal deaths of white persons and of 45.23 per cent. of black.

Of the 4,000 women under consideration, there were 1,839 white and 2,161 black women in whom a positive Wassermann reaction was present in 2.48 and 16.29 per cent., respectively. There were 105 additional women in whom the Wassermann reaction was negative, but in whose histories syphilis was mentioned. These women were divided into three groups according to amount of treatment before delivery: (1) no treatment; (2) inefficient treatment, and (3) four to six injections of arsphenamin and mercurial treatment with the result that the Wassermann reaction became negative and remained so. In these three categories there were 157, 103 and 163 patients, respectively, and the results of the treatment are shown by the fact that in the first group 52 per cent. of the children were born dead or presented some evidence of syphilis, as compared with 37 per cent. in the second group and 7.4 in the third.

All obstetric patients should be encouraged to register not later than the third or fourth month of pregnancy, a routine Wassermann test should be made at the first visit and in case the result is positive, intensive treatment should be started immediately. In this way syphilis will be reduced from the most important cause of fetal death to one of the least frequent.

Zimmerman, Baltimore.

DAS BEHANDLUNGMASS DER REZENTEN LUES (MEASURED TREATMENT OF RECENT SYPHILIS). Alfred Brandweiner, Wien. klin. Wchnschr. **33**:558, 1920; continued **33**:583, 1920; concluded **33**:608, 1920.

A routine treatment for all cases of syphilis cannot be practical. One must consider the individuality of the patient and his infection. Recent syphilis should be divided into two classes: a period prior to the stage of positive serology and a stage after the Wassermann reaction has become positive. Patients of the second class should be regarded as secondary syphilitic patients. The Wassermann test should be made at each vein puncture, and if positive at any time during treatment, the patient belongs to the second class even if the Wassermann reaction before treatment was begun had been negative.

Ideals in treatment have changed with the advent of arsphenamin and the Wassermann reaction. Freedom from clinical symptoms is not enough to judge the efficacy of the therapy, and abortion of infection is possible in the early cases.

Brandweiner used the neosalvarsan brand of arsphenamin in this study, using mercury in conjunction either intramuscularly or by rubbings. In cases in which the diagnosis was made by the demonstration of the *Spirochaete pallida,* treatment was begun with 0.3 or 0.45 gm. The second injection was given after an interval of from five to seven days, and if no untoward results had followed the first, the dose may be 0.6 gm. The mercury treatment is begun after the second neo-arsphenamin injection. The neo injections are contained at weekly intervals, using 0.6 gm. until 26 decigrams have been administered. After an interval of two months the treatment is repeated in all cases to be certain that there be no recurrence either clinically or serologically. In the Wassermann positive cases, a third course is recommended.

Brandweiner studied his cases with the view of determining the relation between the quantity of treatment and recurrences. On an average, the difference of 0.5 gm. of neo-arsphenamin was all that lay between success and failure. For example, thirty-two patients received an average of 2.85 gm. of neo-arsphenamin and remained asymptomatic, while twelve other patients who received an average of 0.325 gm. of the same drug showed secondary manifestations. The mercurial treatment was fourteen rubs and five injections in the first group, and fifteen rubs and five injections in the second.

Neurorecidive lesions may be prevented by local treatment of the chancre. Excision of the lesion and mercurial applications to the site appears to be a procedure to be recommended. If the localization prevents excision, mercury should be applied and kept up even after the sore has disappeared and until all evidence of infiltration has disappeared.

Goodman, New York.

PELLAGRA. Francis D. Boyd, Edinburgh M. J. **24**:6 (June) 1920.

Pellagra is a disease which is of enormous importance from an economic standpoint in Italy, Spain, the Middle East, Lower Egypt, Northern China and other parts of the world. It is estimated that in Roumania alone as many as 100,000 cases of pellagra have occurred in one year. There are far more cases in Great Britain than is generally recognized.

In an inquiry into the health of the Turkish prisoners of war, Boyd and his collaborators found that pellagra was prevalent in November, 1918, over 1,500 patients with this disease being admitted to the hospital.

The characteristic early features of the disease are pigmentation and dryness of the skin. The pigmentation and dryness were first noticeable on the backs of the hands and on the face. On the face, commencing on the nose, it spread out over the cheek in a bat-wing outline. There was a band of pigmentation around the neck and extending down the sternum like a cravat. The dorsa of the feet showed dryness and pigmentation. Points of pressure showed pigmentation and scars were deeply pigmented. In acute cases the pigmentation developed into erythema, and even into ulceration. The backs of the hands appeared raw and deep cracks developed. The appearance of the tongue was characteristic. At first somewhat furred, it rapidly lost the epithelium and had the appearance of moist raw meat.

Early in the disease the hydrochloric acid of the stomach was diminished, to become completely lost in the fully developed clinical picture. The systolic blood pressure was found to fall as low as 78 in acute cases.

As a result of the clinical and laboratory studies, Boyd concludes: (1) that the clinical features of the disease are those of profound suprarenal inadequacy; (2) that there is no evidence of any specific protozoan or bacterial infection; (3) that digestive disturbance accompanied by defective secretion of hydrochloric acid leads to disturbance of pancreatic functions, defective digestion, and malassimilation of protein and fat; (4) that there appears to be an intimate connection between biologic protein in the diet and pellagra; (5) that the disease produces a loss of resistance to the invasion of bacterial and protozoan disease, and is therefore a contributory factor to a high rate of mortality.

Levin, New York.

CHRONIC FIBROID SUBCUTANEOUS SYPHILOMATA OF THE LEGS, ASSOCIATED WITH CHRONIC PERI-URETHRAL INDURATION IN THE PENIS (SO-CALLED "INDURATIO PENIS PLASTICA"). F. Parkes Weber, Brit. J. Dermat. & Syph. **32**:173 (June) 1920.

Weber describes the case of a man, aged 60 years, who had had gonorrhea at the age of 20, and who had a positive Wassermann reaction, although there was no history of syphilis. There was a peri-urethral nodular infiltration in the distal half of the penis, apparently situated in the fibrous tissue of the septum between the corpora cavernosa. The patient likewise presented multiple subcutaneous, rather hard nodules on his lower extremities. The nodules were painless and hardly tender to pressure, varying in size from a hazelnut to a chestnut. These had been present for seven or eight years, one of the nodules, lying deep in the subcutaneous fat and close to, though not actually adherent to the capsule of the knee-joint. Macroscopically it seemed to consist of hard, white fibrous tissue, irregular in outline, and not encapsulated. Microscopically there was seen a dense mass of fibrous tissue, surrounded by and including numerous foci of chronic inflammatory small cell infiltrations.

Weber thinks that this proves that the growths are not true fibromas, and that they are due to some kind of chronic inflammation, probably syphilitic, and he interprets them as probably tertiary syphilitic gummas which have become fibrous without undergoing a true gummatous or necrotic change. For the author the chief interest in this case lies in the association of the subcutaneous chronic fibroid syphilomas of the legs with the chronic peri-urethral induration in the penis, for he considers that the latter condition may also be in some cases a fibrous change of syphilitic origin. He discusses this chronic peri-urethral induration in detail.

Senear, Chicago.

DIE PATHOLOGIE UND THERAPIE DER SYPHILIS IM LICHTE DER MODERNEN FORSCHUNGSERGEBNISSE (THE PATHOLOGY AND TREATMENT OF SYPHILIS IN THE LIGHT OF MODERN INVESTIGATIONS). E. Finger, Wien. klin. Wchnschr. **33**:*373*, 1920.

A presentation of the advances in the knowledge of the bacteriology, serology and specific medication of syphilis. The value of clinical knowledge of early syphilis is emphasized, and the correlation of laboratory and physical examination is insisted on. In primary syphilis prior to the Wassermann positive period, treatment consists of thirty mercury rubs, or ten injections of mercury salicylate or calomel, and five or six moderate doses of arsphenamin or neo-arsphenamin. Ordinarily this suffices, although it is a good measure to examine the blood by the Wassermann test. Once the Wassermann reaction is positive, even if no secondary symptoms are apparent, the case is to be considered one of secondary syphilis. The treatment in this stage consists in repeated courses of arsphenamin and mercury at intervals of three or at most four months. In some cases of failure to reduce the Wassermann reaction by arsphenamin and mercury, success may follow the injection of milk and other substances which induce a temporary rise in temperature. If the spinal fluid reaction is positive, efforts should be made by intensive treatment to negative the abnormal findings. Intraspinous treatment is still questionable. The new advances in the pathology of syphilis are bringing up problems in treatment that are still beyond our knowledge.

Goodman, New York.

MALADIE CUTANEE PROVOQUEE PAR UN PEDICULOIDES TROUVE DANS UN CHARGEMENT D'ORGE ARRIVANT AU HAVRE (CUTANEOUS DISORDER PRODUCED BY A PEDICULOIDES FOUND IN A CARGO OF BARLEY RECEIVED AT HAVRE). Loir and Legangneux, Paris méd. **10**:140 (March) 1920.

Loir and Legangneux describe an outbreak of an eruption among men engaged in unloading barley from a Japanese vessel. Sixty-three men developed the eruption which affected the covered parts, and it was found that in those wearing a belt the thighs were not affected, while the opposite was true among those wearing suspenders. Sacks of wheat had first been unloaded from the vessel without incident, and it was only after they had unloaded barley that the men began to complain of intense itching. Examination of the barley and the dust from the sacks disclosed a parasite belonging to the family of Tarsonemidae and to the group of Pediculöides. Under antiscabetic treatment improvement was rapid and sulphur fumigation of the cargo prevented further outbreaks of the eruption at Havre. The authors review the record of outbreaks of like nature at Havre, and in conclusion give directions for preventing future attacks.

Senear, Chicago.

THE RELATIONSHIP BETWEEN ARSENICAL POISONING AND YPERITIS. J. E. R. McDonagh, Brit. J. Dermat. & Syph. **32**:188 (June) 1920.

McDonagh notes that in cases of arsenical and mustard-gas poisoning three points common to both stand out: 1. The delayed onset of symptoms of intoxication. 2. The fact that such symptoms may vanish and then reappear. 3. The frequency with which a bacterial infection complicates the worst cases.

After a detailed and highly technical comparison of these two conditions he concludes that:

1. Arsenic is the cause of arseno-benzene poisoning, and sulphur of mustard-gas poisoning.
2. Arsenic and sulphur act as catalysts, which fact prevents their ready excretion and induces the recurrence of the symptoms of intoxication.
3. Metals and non-metals are antidotes for each other.
4. Metals and non-metals act therapeutically through the host's resisting substance, which latter they destroy if prescribed in overdose, thereby enabling other organisms which are normally kept in check to multiply until they kill the patient.

Senear, Chicago.

ECZEMA OF THE VERMILION BORDER OF THE LIPS. Douglass W. Montgomery and George D. Culver, Med. Rec. **98**:141 (July) 1920.

The authors are not sure that any of the cases were of a true eczema type. They divided the various types into:

1. Catarrhal inflammation of the red of the upper lip. This condition often leads to swelling and deformity as a result of pyogenic infection and is commonly found in the tuberculous. Soothing antiseptic applications serve best as local treatment.
2. Eczema of the lips as occurring in those with exudative diathesis. In these the lower lip is unduly prominent and frequently desquamative or herpetic with a tendency to fissure formation. These cases require constitutional treatment. The local applications are dependent on the existing condition; if the cracking is deep 60 per cent. lead plaster and 2 per cent. salicylic acid are used, or if there is much infiltration and they are of long standing radium is preferable.
3. The scurfy, scaly lip of the outdoor worker. In these the lips are dry, commonly scaly and tend to crack. This condition is most satisfactorily treated with radium.

4. Patches of hyperkeratosis. These resemble keratotic conditions on other parts and are commonly associated with them. They are also best treated with radium.

Tomlinson, Omaha.

HYPOPHYSIS AND SCLERODERMA. Guido Izar, Riforma med. **36**:482 (May 22) 1920.

The author makes a general survey of the literature of scleroderma and points to its relation to disturbances of the internal secretions, chiefly of the hypophysis. He relates the case of a girl, 7 years old, who presented a localized scleroderma of the right hand rapidly spreading to the rest of the body, being more marked on the neck and thorax. Provocative injections of epinephrin, atropin, thymus, ovarian and thyroid substances, produced no reaction. On the contrary, the injection of 0.25 and 0.5 c.c. of pituitary extract and hypophysin, produced a rise in temperature, increased blood pressure (from 70 to 108) and caused the pulse rate to become slow. Roentgen-ray examination of the skull showed an enlarged sella turcica, measuring 19 mm. by 7 mm.

The patient was treated with injections of pituitary extract and hypophysin on alternate days. After the sixth injection the condition began to improve and eight months later the patient had recovered. Only a few small areas of atrophic skin remained on the nape of the neck and on the wrist.

V. Pardo-Castello, Havana.

COMMENT LES INDIGENES MAROCAINS SUIVENT LE TRAITEMENT DU LECHBA (HOW THE NATIVE MOROCCOANS FOLLOW THE TREATMENT OF LECHBA). Pouponneau, Paris méd. **10**:145 (March) 1920.

Under the heading of medical curiosities, Pouponneau describes the devotion of the native Moroccoans to the so-called lechba treatment for syphilis, which they continue to use in spite of the fact that intelligent treatment is offered them free. The generic term "lechba" includes a number of old methods of treatment based on a vegetable régime. Not only syphilis and everything connected with it is thus treated, but many unrelated conditions as well.

The Lechba el Aoud, employed in the treatment of the graver accidents of secondary syphilis, employs sarsaparilla root, while the Lechba el Iazir, less active, and used for syphilitic headache, arthritis, etc., employs *romarin* leaves.

Pouponneau describes in detail the method of carrying out these treatments.

Senear, Chicago.

UEBER DIE GOLDSOLREAKTION IM LIQUOR SYPHILITISCHER, DAS VERHALTEN ZU ANDEREN LIQUORREAKTIONEN AND IHRE KLINISCHE BRAUCHBARKEIT UND BEDEUTUNG (THE COLLOIDAL GOLD REACTION OF THE CEREBROSPINAL FLUID IN SYPHILITICS, ITS RELATION TO OTHER CEREBROSPINAL FLUID REACTION AND ITS CLINICAL VALUE AND APPLICABILITY). J. Kyrle, R. Braunt and F. Mras, Wien. klin. Wchnschr. **33**:1, 1920.

The cerebrospinal fluid of the early syphilitic patient may show changes in constitution before any clinical signs are evident. These changes are not gross, but are of a complicated physicochemical nature.

The authors have examined 720 fluids. Unfortunately, they do not give the colloidal gold curve in full for their cases, merely indicating the reaction as —, ±, +, ++, +++. The cases were divided into nine groups from the seronegative primary syphilitic cases progressively to cases with tertiary clinical manifestations. The colloidal gold reaction was found to parallel, for the most part, the Wassermann reaction and the globulin findings. In many instances it was found to precede other positive tests and to indicate grave changes in the cerebrospinal fluid.

Reversals to negative findings are difficult to secure, despite vigorous therapeutic measures.

Goodman, New York.

STUDIES ON PIGMENT WITH THE DOPA-REACTION, ESPECIALLY IN CASES OF VITILIGO. Arne Kissmeyer, Brit. J. Dermat. & Syph. **32**:156 (May) 1920.

Kissmeyer reviews Block's work with the "dopa-reaction," and then relates the result of its use in cases of vitiligo. He found that the pigmented portion of the skin gave a pronounced dopa-reaction, and was thus sharply demarcated from the nonreacting achromic portion of the skin. Microphotographs showing this, together with the apparent function of the dendritic pigment cells (melanoblasts of Block) are shown. Considering Bloch's theory of pigment production and his investigations, Kissmeyer concludes that the pathologic process in vitiligo is as follows:

"The vitiligo is an exhaustion dermatosis (Aufbrauchsdermatose), where the dopa-oxydase is used up on account of some unknown stimulant. In the extension of the process some cells or cell groups, which still react, are left in the achromic skin. By the very strong stimulation of the carbon arc-light baths the cells are induced to a more active dopa-oxydase production and the melanoblasts especially become very active; from the spots already pigmented they move into the achromic skin. It is not quite clear what their later destiny is. If they disappear after giving up their pigment (and oxydase?) to the cubical cells or if they themselves are changed into fixed epidermal cells is a question not yet clearly answered. That their rôle in pigment formation is a very important one is unquestionable.

Senear, Chicago.

THE FALLACY OF DEEP "IONIC MEDICATION." W. J. Turrell, Am. J. Electrotherap. & Radiol. **38**:229 (July) 1920.

Ionic medication is defined as the attempt to obtain the specific action of certain drugs introduced into the tissues by means of the electric current. The writer states that the most direct proof against deep ionic medication is to be found in the failure to detect the presence of the drug deeper than the superficial layers of the skin after careful and thorough experimentation. He also maintains that the results obtained in ionic medication are not specific drug reactions, but are due to the electrolytic action of the galvanic current and that they are similar whether expensive drugs or common salt are employed for the solutions. Turrell states that this theory was sponsored in the eighteenth century and that its revival in the present day has led to much quackery prejudicial to the status of electrotherapy.

H. R. Foerster, Milwaukee.

THE ALKALI RESERVE IN PELLAGRA. M. X. Sullivan and R. E. Stanton, Arch. Int. Med. **26**:41 (July) 1920.

Examinations were made of fifty-six patients with pellagra in various stages using no medication and varying the diet only. They were tested for alkali reserve by the alveolar air method and by the determination of the carbon dioxid bound by the blood plasma. None showed marked depletion of the alkali reserve, about one-third were slightly below normal; the majority were within normal limits. The authors conclude from this work that there would seem to be little uncompensated acidosis in pellagra.

Jamieson, Detroit.

STUDIES ON THE EFFECT OF LIGHT ON VITILIGO. Carl With, Brit. J. Dermat. & Syph. **32**:145 (May) 1920.

With's attention was called to the relation of vitiligo to light while working with light baths in the Finsen Institute. As a result of studies carried out he concludes:

1. During carbon arc-light baths vitiligo becomes visible in regions where formerly it was difficult to perceive; we have, on the other hand, not succeeded in producing new spots of vitiligo.
2. The carbon arc light produces on the patches of vitiligo a more or less decided macular pigmentation; this spreads from the periphery to the center, and may last fourteen months.
3. In three cases this pigmentary process continued after the light bath had ceased.
4. The vitiligo patches react with a stronger erythema than the pigmented skin, but little by little the patients are able to stand a quantity of light to which they formerly reacted with an erythema, not only on the pigmented but also on the vitiliginous regions of the skin. Consequently the organism is capable of protecting itself against the light in another way than by pigmentation.
5. The final proof has not yet been forthcoming that the rôle of the pigmentation is to form a protection against light. So many observations, however, tend to show that it must be considered as the most probable deduction.

Senear, Chicago.

PHYSIOTHERAPY IN THE TREATMENT OF CHRONIC SKIN DISEASES. J. M. E. Prevost, Am. J. Electrotherap. & Radiol. **38**:235 (July) 1920.

As physiotherapeutic agents the writer names vibrotherapy, the static breeze, high frequency sparks and effluves, bi-electrolysis, hydro-electric baths, luminous baths, actinotherapy and the roentgen rays. The writer states that because of its efficiency against the cellular perversions of metabolism, physiotherapy ranks first in the rational curve of skin conditions. The roentgen rays are lauded in the treatment of hypertrichosis, nevus pigmentosus, trichophytosis and alopecia, but are otherwise given scant mention.

The other agents are enthusiastically referred to in the treatment of such conditions as nevi, acne, psoriasis, eczema, pruritis, sycosis, cancroids of the face and erythemas.

H. R. Foerster, Milwaukee.

NEOSALVARSANFALSCHUNGEN (SPURIOUS NEOSALVARSAN). L. ARZT, Wien. klin. Wchnschr. **33**:451, 1920.

There seems to be an organized trade in brands of spurious neosalvarsan, and the ampules, labels and containers, even to the seal have been cleverly counterfeited. In several instances, a number of original neosalvarsan tubes had been mixed with the others. [No doubt some of these products have reached this country. Physicians should take warning and not purchase so-called neosalvarsan of German make that is supposed to have been brought over by sea captains and the like. Recently I saw a doctor, who had purchased some of the "real" neosalvarsan, try to dissolve the stuff. A thick custard-like emulsion was the result. At the time of purchase, the seller had made a solution from another ampoule.]

GOODMAN, New York.

UEBER DIE NEUEN AUSFLOCKUNGSREAKTIONEN ZUR LUESDIAGNOSTIK IN BLUT UND LIQUOR (RECENT PRECIPITATION TESTS ON BLOOD AND CEREBROSPINAL FLUID IN SYPHILIS). KAFKA, Dermat. wchnschr. **70**:385 (June 19) 1920.

Kafka discusses the technic of the Sachs-Georgi and the Meinecke tests. He describes with illustrations a new agglutinoscope for more exact reading of results. Both tests corresponded with the Wassermann in approximately 95 per cent. of the examinations. The Sachs-Georgi test seemed to be more sensitive in cases of primary syphilis and in treated cases. Kafka emphasizes the fact that these tests do not replace the Wassermann, but must be used in conjunction with it.

ZIMMERMAN, Baltimore.

ROENTGENOGRAPHIC APPEARANCE, DIAGNOSIS AND PATHOLOGY OF SOME OBSCURE CASES OF BONE LESIONS. ROBERT W. LOVETT and S. B. WOLBACH, Surg., Gynec. & Obst. **31**:111 (Aug.) 1920.

Syphilis affects bones in two ways and results either in the destruction or the new formation of bone. Both are effects of the proliferative reaction to the causal agent, and both may occur in the same case. Destruction of bone follows the local, rapid formation of gummatous lesions, sometimes of endosteal and periosteal origin, sometimes perivascular and extending into bone. On the other hand, the degree of reaction of the spirochetes may be slight and result only in proliferation of cells of the periosteum and endosteum, the newly formed tissue developing osteoblasts and eventually, resulting in new deposits of bone. In one case, therefore, there is choking of normal bone by the gummatous process with its necrosis; in the other, merely stimulation of bone-forming tissue.

GOODMAN, New York.

ZUR ABORTIVBEHANDLUNG DER SYPHILIS (THE ABORTIVE TREATMENT OF SYPHILIS). LEVEN, Dermat. wchnschr. **70**:369 (June 12) 1920.

Leven protests against the dogmatic statement that cases of seronegative primary syphilis can be aborted by a single course of treatment. He cites the case of a patient treated with seven injections of the neosalvarsan brand of arsphenamin and thirty-two inunctions who developed a neurorecurrence shortly after cessation of treatment. A second patient developed a reinduration three and one-half weeks after a course of ten 0.3 gm. doses of natrium-salvarsan.

Zimmerman, Baltimore.

DIMAZON TO PROMOTE THE GROWTH OF HAIR. I. Saudek, Dermat. Centralbl. (May) 1920.

For eight years Dr. Saudek has been using dimazon in the treatment of alopecia areata. He has treated forty cases of the disease with this drug. In two to three weeks, he claims, the hair begins to return. Even in cases of alopecia following seborrhea the hair is regenerated to a certain extent. In ten cases of alopecia following influenza he thought that this drug hastened the return of the hair. He uses it in a 2 per cent. ointment and directs that it be thoroughly massaged into the bald areas, twice daily. He did not use the ultraviolet rays in any of these cases, but suggests that the combined use of these remedies may give even better results

Heithaus, Cleveland.

KERATODERMA BLENNORRHAGICA: IS IT A FORM OF PSORIASIS? H. G. Adamson, Brit. J. Dermat. & Syph. **32**:183 (June) 1920.

Adamson saw several cases in which patients suffering with rheumatoid arthritis associated with more or less extensive psoriasis of the limbs and trunk, had heaped-up horny looking lesions of the palms and soles, bearing a close resemblance to the horny-looking cones of gonorrheal hyperkeratosis. Coupling this observation with the fact that in many cases of keratoderma blennorrhagica psoriasis or a psoriasiform eruption on the other parts of the body had been noted, and recalling the similar microscopic pictures in the two conditions, he speculates on the possibility that psoriasis may be due to some micro-organism bearing a family relationship with the gonococcus.

Senear, Chicago.

THE INFLUENCE OF ROENTGEN RAYS IN THE DISEASES OF THE SKIN. Jay Frank Schamberg, Am. J. Electrotherap. & Radiol. **38**:239 (July) 1920.

This article is a concise, authoritative review on this subject. A note of warning is sounded regarding persistent treatment with the roentgen ray of any condition which fails to respond. The author points out that vascular changes with resulting devitalization of tissues is likely to result, rendering other methods of treatment ineffective. Filtered rays are advocated in the treatment of herpes zoster in preference to galvanism.

H. R. Foerster, Milwaukee.

LE NEURALGIE SCIATIQUE D'ORIGINE SYPHILITIQUE (SCIATICA OF SYPHILITIC ORIGIN). G. Boudet, Gaz. d. hop. **93**:727, 1920.

In 150 soldiers with sciatica, excluding all cases that might be ascribed to trauma or to a neurosis, the Wassermann test was found to be positive in 38.66 per cent. Clinically the sciatica due to syphilis does not differ from that of other origin; however, the following points suggest syphilis; nocturnal exacerbation, pain in the distribution of other nerves than the sciatic and chronicity. No data as to spinal fluid examination are given.

Zimmerman, Baltimore.

LATE HEREDITARY SYPHILIS. MEMBRANOUS PERICOLITIS, PERIENTERITIS, OR CHRONIC ABDOMINAL SYNDROME. M. R. Castex and Delfor Del Valle, Surg., Gynec. & Obst. **31**:160 (Aug.) 1920.

As the result of medical and surgical studies in Argentina, the authors conclude that hereditary syphilis is a very frequent—perhaps the most frequent—cause of membranous perienteritis and analogous conditions, as described by Lane, Jackson, Wilms and others. It is to be noted that although the efficacy of mercurial treatment had been noted, syphilis, either acquired or hereditary, had never previously been mentioned as a possible cause of this condition.

Goodman, New York.

A SYPHILIZED FAMILY. G. R. Hamilton, Brit. J. Dermat. & Syph. **32**:163 (May) 1920.

Hamilton saw a boy aged 10 years, who had a mixed eruption of psoriasis and syphilis. The Wassermann reaction was positive. Investigation showed the father and the two youngest children had negative Wassermann reactions, while the mother and three older children all had positive reactions. The question as to whether the condition in the children was acquired or congenital arises. The three infected children had all had "tonsillitis" about six weeks before the boy was first seen, but otherwise there were no signs or history of syphilis in any one except the first patient. It is the author's opinion that the condition in the children was acquired.

Senear, Chicago.

A CASE OF OCULAR PEMPHIGUGS. William Campbell Posey, Am. J. Ophth. **3**:507 (July) 1920.

Posey reports a case in a young adult colored woman, associated with a chronic recurrent dermatitis, which had been diagnosed as Duhring's disease by two dermatologists. Clinical records are presented for both the eye and skin condition, and it is noted that the latter was associated with mucous membrane lesions of the mouth and lips. The author does not dispute the dermatologic diagnosis, considering the differentiation of pemphigus and dermatitis herpetiformis as chiefly an academic question.

H. R. Foerster, Milwaukee.

UEBER EINEN UEBERGANGSFALL ZUR SCABIES NORWEGICA (A TRANSITIONAL CASE OF SCABIES NORWEGICA). L. Kumer, Wien. klin. Wchnschr. **33**:271, 1920.

Although Boeck described so-called scabies norwegica in 1848, only fifty cases have been found in the literature. Kumer had the opportunity of studying a case of progressive muscular dystrophy in which scabies was present. The lesions in the palm approximated those seen in Norwegian scabies, especially in the number of burrows present, and the comparative ease of demonstrating the ova. In the histologic sections, from four to six burrows were demonstrable in each centimeter of tissue. The patient also presented the picture of ordinary scabies.

Goodman, New York.

DIE MALIGNE ENTARTUNG VON SALVARSAN-HG-EXANTHEMEN —EXFOLIIERENDE GENERALISIERTE ERYTHRODEMIE (A MALIGNANT FORM OF SALVARSAN-MERCURY DERMATOSES—GENERAL EXFOLIATIVE DERMATITIS). Hermann, Dermat. wchnschr. **70**:401 (June 26) 1920.

Hermann reports the case of a dermatitis, developing after combined treatment with the neosalvarsan brand of arsphenamin and mercury, which assumed all the characteristics of an "erythrodermie exfoliante generalisée secondaire" of Brocq.

Zimmermann, Baltimore.

LES "PILULES DE DUPUYTREN" (DUPUYTREN'S PILLS). R. A. Gutman, Paris méd. **10**:138 (March) 1920.

Gutman gives the various formulas and modifications for Dupuytren's pills, and publishes an autographed prescription of Dupuytren's which was apparently written before 1832 and probably represents the original and unedited formula for these pills, as follows: Extract of guaiac, 4 grains; extract of fumaria, 4 grains; aqueous extract of opium, ½ grain, and mercuric chlorid, ¼ grain.

Senear, Chicago.

ZUR SERODIAGNOSE DER LUES MITTELST NEUERER PRAEZIPITATIONSREAKTIONEN (SERODIAGNOSIS OF SYPHILIS BY NEW PRECIPITATION REACTIONS). L. Kirschner and J. Segall, Wien. klin. Wchnschr. **33**:377, 1920.

The authors have used the precipitation test of Sachs and Georgi in conjunction with the Wassermann test in about 1,000 cases. They believe that it has a certain value in latent syphilis.

Goodman, New York.

MERCURY BICHLORID INTRAVENOUSLY. C. H. Bastron, Am. J. Med. Sc. **160**:118 (July) 1920.

In cases in which quick results must be obtained the author advocates using mercuric chlorid in normal salt solution, giving 0.1 of a grain two or three times weekly, increasing the dose slowly up to a point short of salivation. The greatest danger to be avoided is thrombosis. This can be lessened by suspension of the mercury in serum before injection.

Jamieson, Detroit.

A CASE OF KERATODERMA BLENNORRHAGICA IN A WOMAN. C. Leonard Isaac, Brit. J. Dermat. & Syph. **32**:195 (June) 1920.

This clinical note records a case of keratoderma blennorrhagica which is unusual in that the patient was a woman. Graham Little, in 1918, drew attention to the fact that no authentic case had been observed in a woman.

Senear, Chicago.

UEBER EINIGE HAUTVERAENDERUNGEN BEI TIEREN (SOME SKIN CHANGES IN ANIMALS). B. Lipschutz, Wien. klin. Wchnschr. **33**:426, 1920.

A presentation of animals with affections of the skin. Scabies of rats, and molluscum contagiosum of pigeons were among those demonstrated.

Goodman, New York.

THE EFFECTS OF TUBERCULIN IN LUPUS VULGARIS. Robert Aitken, Edinburgh M. J. **24**:4 (April) 1920.

In view of the fact that statements have been made that in the treatment of lupus vulgaris tuberculin not only does no good, but interferes with the efficacy of other remedies, the writer, at the request of Dr. Norman Walker, investigated the cases which had been so treated.

The cases reviewed fall into two main classes, namely, those treated exclusively with Koch's New Tuberculin (T. R.) and those in which Koch's Original Tuberculin (O. T.) was given. All patients improved, even those who received a short course of tuberculin. The drug is not held out as the only way of curing lupus, nor as the best way of treating all patients, but there does not seem to be any evidence in the series of cases under review that the injections prevented any other remedy doing good.

Levin, New York.

ROENTGEN-RAY TREATMENT OF VERRUCAE PLANTARIS. H. H. Hazen and F. J. Eichenlaub, J. A. M. A. **74**:1311 (May 8) 1920.

The authors report the records of sixteen cases of plantar warts treated by the roentgen ray. Some of those of longest duration responded most quickly to treatment, and neither size nor location appeared to play any part. Almost invariably the pain disappeared in from two to four days after the first treatment. Their technic is to give 1½ Holzknecht skin units every three or four weeks, the dosage being estimated according to the method long advocated by MacKee. When the lesion has disappeared, they usually give an additional treatment to be sure of a complete cure. They use no filter in this work, as they feel that on superficial lesions results are much better with the unfiltered ray. The cure seems to be permanent.

Waugh, Chicago.

UEBER DEN KLINISCHEN WERT DER AUSFLOCKUNGSREACTION NACH SACHS UND GEORGI (CLINICAL VALUE OF SACHS-GEORGI PRECIPITATION REACTION). Ludwig Kleeberg, Dermat. Wchnschr. **70**:33 (Jan.) 1920.

The Sachs-Georgi and Wassermann tests corresponded in 89.6 per cent. of 1,112 serums examined. In forty-three cases, in which the Wassermann test was positive and the diagnosis of syphilis was unquestionable the Sachs-Georgi reaction was negative. Sixteen of the patients presented secondary lesions; in the thirteen which returned for reexamination the Sachs-Georgi reaction subsequently became positive. In six cases of secondary syphilis the Wassermann test was negative, the Sachs-Georgi positive. In six cases of tertiary syphilis and parasyphilis the Wassermann test was positive, the

Sachs-Georgi negative; in ten similar cases the Sachs-Georgi was positive, the Wassermann negative. Under treatment the Sachs-Georgi reaction became negative more slowly than the Wassermann.

ZIMMERMANN, Baltimore.

UEBER DIE BEHANDLUNG VON TAETOWIERUNGEN (REMOVAL OF TATTOO MARKS). STUTZMANN, Dermat. Wchnschr. **70**: No. 5 (Jan.) 1920.

After a review of the various methods for removing tattoo marks the author gives his experience in treating a case in which the skin was filled with carbon particles following the explosion of a bomb. The best result was obtained by application of moist pepsin dressings after the affected parts had been subjected to multiple punctures with tattoo needles. This treatment was kept up for seven months after which the dark particles in the skin had assumed a grayish color and in some places seemed to have entirely disappeared.

The author also obtained good results in a tattoo mark by retattooing the area with a 45 per cent. solution of zinc chlorid.

KETRON, Baltimore.

ULCUS TROPICUM TREATED WITH TARTAR EMETIC. A. MEI, J. Trop. M. **23**:38 (Feb. 2) 1920.

In addition to intravenous use, this drug can be applied locally with great efficiency, according to the author. It should be applied carefully to the edges of the ulcer, only a small amount of powder being used. The local reaction may be rather severe, but the organisms begin to disappear in two or three days and are practically gone in two weeks. The spirochetes first disappear, Vincent's bacilli and cocci remaining much longer even though the ulcer improves before they have disappeared. For this reason the author thinks that the *Spirochaeta Schaudinni* is the true etiologic factor and that Vincent's bacilli are symbiotic and have no pathologic significance.

JAMIESON, Detroit.

VENEREAL PROPHYLAXIS. P. M. ASHBURN, J. A. M. A. **74**:1314 (May 8) 1920.

In order to determine, if possible, whether the use of prophylaxis prevents one type of venereal disease more than another, a comparison was made by Ashburn of the relative proportions of the three diseases in the first 2,000 cases in which infection followed the use, and in the first 2,000 cases in which it followed neglect of prophylaxis. The results were: without prophylaxis, gonorrhea, 67.2 per cent.; chancroid, 15.6 per cent.; syphilis, 17.2 per cent.; with prophylaxis, gonorrhea, 64.5 per cent.; chancroid, 18.9 per cent., and syphilis, 16.6 per cent.

WAUGH, Chicago.

ANTHRAX FROM THE SHAVING-BRUSH AND PRIMARY ANTHRAX MENINGITIS. H. W. CAREY, Am. J. Med. Sc. **159**:742 (May) 1920.

Attention is directed to the number of cases of anthrax since 1914, especially in England and in concentration camps. In the case reported the patient was infected without question by a new, cheap shaving brush used for the first time the day before the pustular lesion began. Complete recovery followed excision. Most of the infections were found to be due to the use of horsehair and pig bristles imported from China and Siberia and used in manufacturing shaving brushes. Direct cultural attempts were unsuccessful, due to the large overgrowth of adventitious organisms.

Nine instances of meningeal infection have been reported, of which three were apparently primary. Septicemia and intestinal or pneumonic infection have also occurred.

Jamieson, Detroit.

CAS DE LUPUS ERYTHEMATEUX PLANTAIRE (CASE OF PLANTAR ERYTHEMATOUS LUPUS). Parin and Périn, Bull. Soc. franç. dermat. et syph. No. 8, 1919.

Parin and Périn describe a case of lupus erythematosus in which typical lesions of the face and hands are associated with lesions on the soles. The lesions in the latter site are described in detail, and have some points in common with lupus erythematosus of the face, although the general aspect is different. The diagnosis was also supported by microscopic examination of the excised tissue.

Senear, Chicago.

UEBER DIE UEBERTRAGBARKEIT DES HERPES SIMPLEX AUF DIE KANINCHENHORNHAUT (THE TRANSMISSION OF HERPES SIMPLEX TO CORNEA OF RABBITS). Oskar Baum, Dermat. Wchnschr. **70**:105 (Feb.) 1920.

This work is a repetition of that of Löwenstein who was able to transmit herpes simplex in fourteen instances to the corneas of rabbits (*München. med. Wchnschr.*, 1919, No. 28). Baum was successful in seven cases and in one instance transmitted the disease from the cornea of one rabbit to that of another. He was unable, however, to transmit in a like manner other vesicular conditions, such as herpes zoster, eczema, pemphigus, etc. The author believes that the inability to transmit herpes zoster speaks for the sharp differentiation of this disease from herpes simplex.

Ketron, Baltimore.

UNSERE ERFAHRUNGEN MIT SULFOXYLAT (EXPERIENCES WITH SULPHOXYLAT). Gustav Fantl, Dermat. Wchnschr. **70**: 155 (March) 1920.

Sulphoxylat, a new arsphenamin derivative made by Kolle, was found to be inferior to arsphenamin in its sterilizing power. In some cases repeated doses were necessary to cause the disappearance of spirochetes from lesions.

Zimmermann, Baltimore.

MEINE BEHANDLUNG DER TRICHOPHYTIA UND SYCOSIS BARBAE (MY TREATMENT OF TRICHOPHYTOSIS AND SYCOSIS BARBAE). J. Wetterer, Dermat. Wchnschr. **70**:87 (Feb.) 1920.

The treatment consists of various combinations of antiseptics, ultraviolet light, roentgen ray and electrolysis, depending on the type of disease treated. The author claims cure in 98 per cent. of cases. For detail of treatment the reader should consult original article.

Ketron, Baltimore.

CASE OF APPARENT DIPHTHEROID INFECTION OF THE SKIN. H. W. BARBER, Proc. Roy. Soc. Med. **13**:40 (March) 1920.

Beginning as a boil on the dorsum of the left wrist, the patient developed spreading lesions on the left forearm, right calf and left leg. The Wassermann reaction and repeated examinations for the streptothrix and sporothrix were negative. Finally a diphtheroid organism was isolated from the deep skin layers which proved pathogenic to animals and was agglutinated by the patient's serum. After repeated failures by different lines of therapy, an autogenous vaccine was given and the patient made a rapid recovery.

GUY, Pittsburgh.

THE CEREBROSPINAL FLUID IN MULTIPLE SCLEROSIS. J. E. MOORE, Arch. Int. Med. **25**:58 (Jan.) 1920.

On account of the frequency of finding a "paretic" colloidal gold curve in cases of multiple sclerosis, the writer has analyzed the spinal fluid findings in twenty-eight cases showing that the curve mentioned is not typically syphilitic with other findings negative. Sixteen of these cases showed a pleocytosis (above 5); globulin was positive in twenty-five, while blood and spinal fluid Wassermann reactions were negative. Eighteen cases showed a paretic gold curve, seven were negative and three syphilitic.

He thinks the picture presented in these spinal fluid findings is strong evidence of multiple sclerosis.

JAMIESON, Detroit.

THE ROENTGEN-RAY TREATMENT OF VERRUCA PLANTARIS. H. H. HAZEN, J. A. M. A. **74**:19 (May 8) 1920.

Sixteen cases of verruca plantaris were treated by the roentgen ray with success and apparent permanent cure. The technic consisted in giving 11/3 Holzknecht skin units every three to four weeks. From two to seven treatments were given to obtain a cure.

LEVIN, New York.

CASE OF ERYTHEMA INDURATUM IN YOUNG GIRLS, ASSOCIATED WITH FOLLICLIS AND PHLYCTENULAR ULCERS. GEORGE PERNET, Proc. Roy. Soc. Med. **13**:53 (March) 1920.

This article discusses a case of Bazin's disease affecting the right calf and associated with folliclis lesions on the back of the hands, phlyctenular ulcers and chilblains. There were two patients with active tuberculosis in the family. It was proposed to give the patient chaulmoogra oil treatment.

GUY, Pittsburgh.

SADD DERMATITIS. A. J. CHALMERS and A. F. JOSEPH, J. Trop. M. **23**:57 (March 1) 1920

This dermatitis is an irritating, small papular eruption caused by coming in contact with small hairs which grow on certain grass in the upper Nile region. The action is purely local and probably entirely mechanical, although the hairs are hollow and may contain a toxin. Thorough removal with soap and water followed by a bland lotion will quickly cure the condition.

Jamieson, Detroit.

UEBER BEOBACHTUNG VON SPIROCHAETEN IM HAENGENDEN TROPFEN BEI DUNKELFELDBELEUCHTUNG (OBSERVATION OF SPIROCHETES IN HANGING DROP PREPARATIONS WITH DARK FIELD ILLUMINATION). F. W. Oelze, Dermat. Wchnschr. **70**:1 (Jan.) 1920.

According to Oelze, this method is especially suitable for the study of motility of spirochetes. A detailed description of the apparatus is given.

Zimmermann, Baltimore.

UEBER EINE HAUSEPIDEMIE VON HAARAUSFALL BEI SAUGLINGEN (A HOSPITAL EPIDEMIC OF LOSS OF HAIR IN INFANTS). Oskar Heller, Dermat. Wchnschr. **70**:145 (March) 1920.

Ten infants from 4 weeks to 6 months of age were affected with a sudden loss of hair during a period of about three weeks. The loss of hair was complete with mild inflammatory reaction, but returned after a short period. No etiologic factor could be determined.

Ketron, Baltimore.

ZUR THERAPIE DER PARAPSORIASIS MIT PILOKARPIN (THE TREATMENT OF PARAPSORIASIS WITH PILOCARPIN). Löwenstein, Dermat. Wchnschr. **70**:4 (Jan.) 1920.

The author describes a case of "parapsoriasis en goutte" cured by the intramuscular injection of pilocarpin hydrochlorid. The first injection consisted of 0.005 gm., the succeeding ones, 0.01 gm. The first five injections were given every other day, the sixth after a five day interval and the last after an eight day interval. Excessive sweating, erythema and occasionally nausea and salivation were observed but there were no alarming symptoms. Eight days after the last injection the disease had entirely disappeared.

Ketron, Baltimore

PHAGEDENA OF HUNTERIAN CHANCRE FOLLOWING TREATMENT WITH NOVARSENOBENZOL. H. M. Hanschell, Brit. M. J. **1**:498 (April 10) 1920.

The author reports two cases of Hunterian chancre, one intra-urethral, the other on the mid-dorsum of the glans penis, in which there was bacterial infection existing with the syphilitic infection. In both cases injections of novarsenobenzol were given, and in both cases gangrene and marked destruction of tissue occurred in the chancre.

He concludes that the effect of the reaction from novarsenobenzol was to damage still further the chancre tissue already damaged by the spirochetes.

Oliver, Chicago.

CASE OF LEPROSY DEMONSTRATING THE VALUE OF A TISSUE VACCINE. A. Winkelried Williams, Proc. Roy. Soc. Med. **13**:50 (March) 1920.

This article concerns a proven case of lepra apparently cured by the use of a vaccine prepared from autogenous lepromas. Dr. Castellani, in discussing the cases, called attention to the fact that Dr. Nichols and he had employed the same technic in 1905 with rather disappointing results. He considered the present improvement evidence of the infection being dormant and spoke favorably of the efficacy of chaulmoogra oil as a palliative.

Guy, Pittsburgh.

SOME FURTHER OBSERVATIONS ON THE ETIOLOGY OF PELLAGRA. A. Viswalingam, J. Trop. M. **23**:46 (Feb. 16) 1920.

The notes given in this article tend to confirm the opinion stated before by the writer that pellagra is primarily a gastro-intestinal disorder induced by low protein diet, unhygienic surroundings, lack of sunlight, etc., followed by an infection which gains entrance through the gastro-intestinal tract.

Jamieson, Detroit.

EIN BEITRAG ZUR SICHTBAREN LYMPHANGITIS TUBERCULOSA (VISIBLE TUBERCULOUS LYMPHANGITIS). Wilhelm Kiendl, Dermat. Wchnschr. **70**: No. 4 (Jan.) 1920.

The author describes, for illustration, a case of tuberculous lymphangitis and gives the differential points between this disease and the lymphangitis of sporotrichosis, syphilis and cancer. He sums up the characteristics of the disease: 1. The presence of a tuberculous "primary lesion" usually lupus, tuberculous ulcer or a postmortem tubercle, or the lymphangitis may be associated with bone or joint tuberculosis. 2. There are palpable, thickened, nodular cords running centrally from the primary lesions. 3. Chronic swelling of the regional lymph gland is often present. 4. If the nodules soften and break through the skin, typical tuberculous ulcers with irregular, undermined edges are formed. 5. The course of the disease is slow and chronic, the fever is slight and there is little pain.

Ketron, Baltimore.

Book Review

OCCUPATIONAL AFFECTIONS OF THE SKIN: THEIR PREVENTION AND TREATMENT WITH AN ACCOUNT OF THE TRADE PROCESSES AND AGENTS WHICH GIVE RISE TO THEM. R. Prosser White, M.D., Ed.M.R.C.S. Second edition with 24 plates. London, H. K. Lewis & Co., 1920. Pp. 360.

White, in the second edition of his excellent publication, gives a volume of discussion of the salient features of the occupational affections of the skin as encountered in his own practice and as gleaned from the literature of other countries. The conditions caused by the industries peculiar to the recent war are included in this volume.

The book is, however, broader in scope than its name implies for the whole subject of dermatoses of external origin is considered. It is, therefore, of special value to the dermatologist who will find in this collected and systematized study a truly remarkable fund of significant information on the diagnosis and differential diagnosis of a highly specialized field. The second edition is far superior to the first; it contains many new features, and a broader consideration of the topics of the earlier edition.

White objects to the terms "eczema" and "dermatitis" as applied to the occupational affections of the skin, and thinks it is more convenient and logical to use the noncommittal word "dermatopathy" or "dermapathy" or the less correct but more usual "dermatosis"—disease of the skin. Any of these terms embrace trade lesions of an eczematous type, as well as dissimilar examples of skin disease caused by various occupations. When possible the name of the offending agent should be prefaced, and when this is uncertain, "traumatic," "occupational" or "professional" should be added.

The effects of lightning, roentgen ray, radium, heat and sun rays with their sequelae are carefully given. Dermatitis venenata is accorded a special chapter, and the modern experimental work on immunization and sensitization with the poison ivy, sumac and nettle is included in the discussion of the anaphylactic origin of this group. The ever increasing importance of such diseases as erysipeloid of Rosenbach, postmortem wart, anthrax, glanders, blastomycosis and the other dermatoses induced by insects and vegetables are mirrored by the liberal space allotted to them. A chapter on war dermatoses and their relation to postbellum civilian practice closes the volume.

There are numerous references, which are thoroughly up to date. About sixty pages of the book are occupied by the index. These features will prove a boon to the inquirer.

Index to Current Literature

DERMATOLOGY

Cancers, Superficial, Actual Cautery in Treatment of. C. F. Sherwin, J. Missouri M. A. **17**:269 (July) 1920.

Carbon Tetrachlorid in Surgery and Dermatology. E. Desesquelle, Bull. méd. **34**:658 (July 24) 1920.

Carcinomas, Superficial, Irradiation of. Seitz and Wintz, München. med. Wchnschr. **67**:145 (Feb. 6) 1920.

Cryotherapy in Dermatology. Lortat-Jacob, Progrès méd. **35**:303 (July 10) 1920.

Dermatitis Caused by Imitation-Leather Sweatbands. Bettmann, München. med. Wchnschr. **67**:291 (March 5) 1920.

Dermatology and Surgery, Carbon Tetrachlorid in. E. Desesquelle, Bull. méd. **34**:658 (July 24) 1920.

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PROTEIN SENSITIZATION IN THE PRODUCTION OF SKIN DISEASE *

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During the last decade there has grown up a voluminous literature on the subject of protein sensitization. Case after case has been reported in which it has been alleged that a skin disease of one form or another has been caused by the ingestion of some food substance. Laboratory workers have been equally busy with the clinicians and they, too, have done their part in adding to the literature.

In reviewing the papers on the various phases of protein sensitization the reader is soon impressed by the multiplicity of the substances accused of toxic action and the resulting anaphylactic shock and equally by the variety of the manifestations which these poisonous substances are alleged to produce. Moreover, the manifestations are not uniform in a given patient even in response to the same toxic stimulus but are various and varied. Neither do the symptoms seem to be constant, for not infrequently a food which was formerly not tolerated later may be innocuous for long intervals.

Prodromal symptoms are equally inconstant and fickle. The anaphylactic shock apparenty develops, often within a few minutes. In other cases it is seemingly delayed even for twenty-four hours or more. In some cases, notably in children, there are constitutional symptoms present in the interval between the poisoning and the reaction which, to the observing mother, indicates the imminence of anaphylactic shock. Nervousness, irritability, loss of appetite, sometimes diarrhea and sometimes fever are common prodromal signs, when such signs occur.

Moreover, many students assert that if the blood be examined at the time of the anaphylactic shock eosinophilia will be found for twenty-four hours or perhaps longer.

As already stated, the response in the skin to the influence of the toxemia is varied. Certain forms of skin manifestations, however, so predominate that in certain quarters they are accepted as satisfactory

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evidence per se of the existence of a state of anaphylaxis, i. e., that they are pathognomonic of anaphylatic shock. Preeminent among these are urticaria, angioneurotic edema and eczema.

Moreover, the dominant testimony of today places bronchial asthma and hay fever in the same category as manifestations of anaphylactic shock. Among many, the belief prevails that bronchial asthma and the skin diseases mentioned are merely variations of the same influence and may appear simultaneously or interchangeably. Therefore, in considering protein sensitization as a cause of skin disease, it is both necessary and illuminating to study the work done in bronchial asthma and hay fever.

One of the most striking facts in connection with the study of protein sensitization is the discovery that in many instances it is possible to detect the offending toxic substance by inoculation or vaccination of the skin. It has been found that when the protein which has sensitized the body is inoculated into the skin certain signs will follow. Moreover, the skin reaction is specific in the sense that the maximum skin reaction occurs only in response to the offending substance.

Even here, however, as will be shown later, all is not clear sailing for just as we have seen the clinical signs vary and even fail, so in response to the food inoculation test the skin does not always react or, if reacting, does so in a manner not explicable by the other evidence present.

It is evident from the foregoing that we are not dealing with a clear cut subject with well defined limits, but rather with a subject in which much work yet remains to be done. This thought has been well expressed by Loewit, whom I take the liberty of quoting.

> So great is the number of alleged shock producing substances and so manifold and changing is the picture drawn of the symptom complex attributed to anaphylaxis and so utterly unconfirmed and so lacking in character are the signs used in diagnosis that either suspicion is aroused of the great multiplicity and instability of the anaphylactic symptom complex or else we can only conclude that many of the processes laid at the door of anaphylaxis really possess only a superficial resemblance.[1]

None can deny that it is difficult to reconcile the changing and confusing claims of the anaphylactic enthusiast with our previous beliefs. The bond between the one time accepted theories and the newer theory of anaphylaxis is not yet complete. We seem to have but one course open to us, either to reject all that we once thought true and accept unreservedly the new theory or to agree with Loewit that the old truths remain unchanged and neither conflict with nor impair the newer facts now coming to light.

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1. Loewit: Ztschr. f. Immunitätsf. **27**:407, 1918.

We can perhaps make the situation clearer if we consider briefly, at this point, one or two clinical histories of typical cases of anaphylactic skin disease.

TYPICAL CASES

Case 1.—First let me summarize Schloss' classic case. A boy, aged 8, had a pronounced idiosyncrasy to eggs, almonds and oats. The previous history is significant in its suggestion of contributing causes leading up to the subsequent anaphylactic developments. The little patient had suffered from seborrheic eczema, mild symptoms of rickets and repeated attacks of the respiratory tract. When 10 days old, the infant had a mild diarrhea for which he was given the white of an egg in barley water. No symptoms whatever followed its administration. When the boy received egg a second time he was 14 months old. Immediately he began to claw his mouth and tongue and the buccal tissues swelled to many times their normal size. Around the mouth typical urticarial wheals developed. Using von Pirquet's borer, Schloss was able to demonstrate the sensitiveness of the skin to egg white by the production of a typical wheal at the site of the inoculation. In the course of further study Schloss showed that the ovomucoid content of the egg white was the specific toxin.

A second case taken from my private records illustrates the multiple protein sensitization that so frequently occurs. It also exhibits the existence of a previous pathologic condition that suggests relationship to the later developing anaphylaxis. Finally, it illustrates the variability and instability of the cutaneous test reaction. The latter is most important as a majority of writers are inclined to accept the behavior of the cutaneous test as evidence of the progress of immunity. All these points will be considered later in greater detail.

Case 2.—A shy, reticent boy of 7 years, while not appearing ill, lacked the activity and robustness of normal boys of like age. The history revealed that he had been well up to 3 years of age. At that time he had a light attack of measles. At first there was nothing noticeable about the attack and the disease followed the ordinary course. As recovery seemed about assured the boy suddenly had a convulsion and for some weeks was seriously ill with meningeal symptoms. When recovery finally came, the boy seemed to have lost all control over both the voluntary and involuntary nervous system. His mind was as clear and keen as ever, but, for example, when he tried to walk he could not make his legs move; when he tried to talk he could not indicate his desire in words although perfectly able to do so in signs. He had to learn all over again to walk and to talk.

From the point of view of the study of protein sensitization, the intolerance which had developed toward foods was most interesting. In Schloss' case just given there was a primary ingestion of a food substance without symptoms followed by sensitization and anaphylactic shock when the antigen, that is, the sensitizing food substance, was taken a second time. In this case, there was no such clear cut story. In his mother's words, the boy was converted from a perfectly normal child who could eat and digest everything given him to a child with a vasomotor system so instable and a digestion sensitized to so many foods that the possible diet was made extremely limited.

Cutaneous food tests were made with the following results: total number of substances tested, 59; total positive reactions, 26; total questionable reactions, 4; total negative tests, 29. The mother also reported her own clinical observations which, as she was more than ordinarily intelligent and observant, may be accepted without reserve. For example, she had learned that while the boy could not eat fresh bread he could eat toast. He could not eat the moist cereals. He could eat the dry cereals, shredded wheat, puffed rice, etc., i. e., those cooked by dry heat. In general, she had learned that foods baked or toasted, that is cooked by dry heat, were less liable to cause anaphylactic shock. Under the mother's careful guidance and by carefully cutting out those foodstuffs that gave a positive result to cutaneous tests, the boy has in the course of four years recovered much of his tolerance toward foods. He still cannot eat everything, but the number of toxic foods has been greatly reduced.

Up to within about a year the anaphylactic reaction manifested itself solely in the lungs. Following the ingestion of anaphylaxis-producing substances the child would have a most distressing asthma with noisy stridor and vomiting. He lost weight and strength during this time. For a year these asthmatic attacks have not been bad. For a year the explosion has manifested itself in the skin almost entirely, the lungs being often not at all or only slightly affected. After a period of irritability the skin breaks out in a generalized guttate eruption resembling both seborrheic eczema and psoriasis.

Preceding the attacks the boy was restless and apprehensive, was afraid to go to bed and would therefore sit up all night. The bowels would also become sluggish. An internist who had been consulted stated, after much study and experimentation, that he was convinced that the lower intestine and the large bowel were characteristically sluggish in functioning and in his opinion had much to do with the production of the anaphylactic state.

Repeated cutaneous food tests were made. During the early months of the case, while the anaphylactic state was at its height, the results were variable. A substance which one day gave a strongly positive reaction, three months later was often found to be negative only to become positive again after another longer or shorter interval. Likewise it was found that substances which when first tested were negative sometimes became, at a later time, positive and remained positive thereafter.

These complicated cases with their multiple figures and changing background at once invite the question, What does it all mean? We must seek the answer in the literature. It is, however, impossible to quote every reference or to consider every phase in detail. Both are too numerous. We can touch but lightly on the many phases of the subject and refer to but a few papers, choosing the most typical and best confirmed for quotation.

CAUSES OF PROTEIN SENSITIZATION

Heredity.—Our search naturally turns first to heredity as a cause of human sensitization. I could find no statistics bearing directly on the anaphylactic manifestations in the skin, but Cooke and Vander Veer [2] give certain suggestive figures for that allied anaphylactic symptom, hay fever.

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[2] Cooke and Vander Veer: J. Immunology, **1**:201, 1916.

They estimate the frequency of human sensitization with clinical manifestations at probably less than 10 per cent. Granted that, as asserted, hay fever is the most frequent manifestation of all anaphylactic phenomena, the frequency with which the skin manifestations occur must be small.

Their figures, with regard to the frequency with which a negative or positive history of sensitization in one or both parents or in a collateral family branch was obtained, are interesting. In sixty-three apparently normal cases, there was a history of sensitization in the father or in the mother in 9.5 per cent. and a positive direct or collateral antecedent history in 14.5 per cent. Among 621 cases of sensitization, the antecedent direct or collateral history was negative in 260; positive in 205; positive on both sides in thirty-nine; that is, in 504 cases out of 621 there was some antecedent history in 48.4 per cent. About 19 per cent of the sensitized persons gave an entirely negative antecedent history. These figures they compare with the 14.5 per cent. positive antecedent histories obtained in normal persons, concluding therefrom that inheritance is a definite factor in sensitization.

Moreover, still speaking of hay fever, their further studies led them to the conclusion that the more complete the inheritance, the earlier the appearance of manifestations in the child. They also concluded that sensitized persons transmit to their offspring not their own specific sensitization, but an unusual capacity for developing bioplastic reactivities to any foreign protein.

These facts and figures are characteristic and are generally accepted by all writers on the subject.

Remembering that hay fever is accepted as the great exponent of anaphylactic manifestations and bearing in mind Cooke and Vander Veer's conclusions as to the transmissibility of protein sensitization, the student will find food for thought in contemplating and comparing Schreier's definition of arthritism or the arthritic diathesis. Schreiber[3] says: "Certain infants are thus born with a 'vice of nutrition' which will manifest itself in them through a specific (individual) reaction to various pathologic agents and will also render them vulnerable to conditions which do not affect the normal organism."

Gastro-Intestinal Diseases and Protein Sensitization.—Enough has already been said to justify a hasty review of current opinion concerning the possible relationship of gastro-intestinal conditions and protein sensitization. Leri[4] maintains that the anaphylactic state and the diatheses possess too many characteristics in common for their similarity to be no more than apparent. Lesné and Dreyfus[5] speak of alimentary anaphylaxis, meaning a process of protein sensitization arising in the alimentary tract. Johnston[6] asserts that "anaphylaxis in the human being commonly expends its force not on the respiratory apparatus but on the gastro-intestinal tract, as is amply proved by cases of serum disease. After all, it matters very little whether indigestion is primary or secondary. It claims attention in either event." Johnston found that hyperacidity occurred more frequently than any other form of digestive disturbance. Sensitization, he says, occurs during the period of frank indigestion.

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[3] Schreiber: Arch. de med. des enfants **15,** No. 6, 1912.

[4] Leri: Ann. de méd. et chir. **16,** No. 22, 1912.

Combe[7] supplements Johnston's views. He says that when the albumins, and especially the fats, in the body are destroyed too rapidly the organism becomes poisoned, a state of acetonemia or acid intoxication resulting. According to Combe, any inflammatory or atrophic changes in the intestinal mucosa favor intestinal putrefaction and hence intestinal toxemias. The same is also true of intestinal stasis.

Dr. V. C. Vaughan[8] furnishes a further hint as to the possible rôle played by the digestive functions in the production of protein sensitization. Writing of the relation of anaphylaxis to immunity and disease, Vaughan says that in producing a state of anaphylaxis or immunity by the injection of certain proteins, the digestive secretions are modified according to the protein used, so that each protein has a specific ferment which acts on no other protein. This process he calls sensitization and states that it may be transmitted to the offspring.

The Liver and Toxemia.—Manwaring[9] found that the liver played an important rôle in general toxemia. In dogs, cutting out the liver from the general circulation also cut out the anaphylactic shock. The reaction, he concludes, occurs chiefly in the liver. Rumpf[10] verified Manwaring's observations by experiments on guinea-pigs, from which he too concluded that the chief effects of the anaphylactic process take place in the liver epithelium.

Combe says that the body has three lines of defense against intoxication and autointoxication, the first being the intestinal mucous membrane, the second the liver and the third the ductless glands. Anything that interferes with the functioning of the liver exposes the organism to invasion by toxins. It is not for nothing, Combe says, that all the blood

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5. Lesné and Dreyfus: Ann. de méd. et chir. **16,** No. 22, 1912.
6. Johnston: J. Cutan. Dis. **30**:96, 1912.
7. Combe: Intestinal Autointoxication, New York, Rebman, 1910.
8. Vaughan, V. C.: Am. J. Med. Sc. **145**:161, 1913.
9. Manwaring: Ztschr. f. Immunitätsf. **8**:1, 1911.
10. Rumpf: Ztschr. f. Immunitätsf. **27**: 1918.

from the intestine must flow through the liver where the liver cells rob it of its poisons. In this, Combe verifies Rumpf and Manwaring.

Ductless Glands and Toxemia.—Janney and Isaacson[11] furnish corroborative testimony as to the value of the ductless glands in the defense of the body from their study of thyroidectomy and thyroid diseases on protein metabolites. Stated briefly, they found that thyroid disease favors protein catabolism thereby linking the thyroid to anaphylactic disease in which, according to the majority of writers, protein catabolism is a prominent feature.

Fordyce writes that owing to the frequent association of urticaria with hay fever and asthma, conditions commonly found in hyperthyroidism, the glands of internal secretion so influence the vessel tone by their products that they form an important factor in the production of anapyhlaxis.

Johnston maintains that the study of a case of urine anaphylaxis in any skin disease is not complete which does not determine the percentage of these bodies (the nitrogen compounds) in the urine. In his experience the most frequent change was a decrease of urea and a corresponding increase in the rest nitrogen fractions, and that when it was marked, symptoms could be looked for.

Eosinophilia.—Among other points most commonly emphasized in the diagnosis of anaphylaxis is the occurrence of eosinophilia. Some writers, indeed, lay so much stress on this phenomenon as to create the impression that they believe it a pathognomonic symptom. Others, perhaps the majority, consider it of lesser importance.

Weinberg and Sequin[13] state that in the anaphylactic process an eosinophilia appears in from one to three days after reinfection of the antigen. They explain the appearance by the hypothesis of a direct irritation of the hemopoietic system by the antigen. Rackemann[14] adopts Staubli's theory to explain that a foreign protein acts as an eosinotactic substance.

These quotations sufficiently illustrate the general trend of opinion.

In contrast to this use of an eosinophilia as a symptom of anaphylaxis is the similar use of eosinophilia as a characteristic of the arthritic diathesis. For example, Schreiber, writing of the diatheses of infancy, quotes Dr. Finkelstein's assistant, Rosenstern, as having brought out a new point in connection with infantile arthritism. Rosenstern says, "Having practiced the examination of the blood of infants suffering from troubles in the skin or mucous membranes of the arthritic series

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11. Janney and Isaacson: Arch. Int. Med. **22**:160 (Aug.) 1918.

12. Fordyce: J. Cutan. Dis. **30**:128, 1912.

13. Weinberg and Sequin: Compt. rend. Soc. de biol. **76**.

14. Rackemann: Arch. Int. Med. **22**:517 (Oct.) 1918.

(eczema, prurigo, asthma, various catarrhs, etc.), I was able to demonstrate an eosinophilia, sometimes reaching 20 per cent." Schreiber therefore concludes that an eosinophilia is common to all diathetic manifestations.

Combe considers an eosinophilia a manifestation confidently to be expected in intoxications and autointoxications.

The questions arise, What value shall we attach to eosinophilia? On eosinophilia as a basis, what relationship shall we assign to protein sensitization and the diatheses and intoxications?

If we turn to a consideration of the prevailing theories of anaphylaxis to help us to a decision we are met with disappointment. In spite of the just expectation that the immense amount of work and research, of which the large and rich literature on the subject is evidence, would yield some definite opinion or standard, we find controversy raging in this field also.

THEORIES OF ANAPHYLAXIS

Humoral Theory.—There are two theories in existence today, the humoral and the cellular. Both have their advocates and their opponents. Friedberger[15] may be taken as a representative of the humoral theory. His theory teaches that the process which results in sensitizing the organisms takes place in the blood. The argument runs that if egg albumin is injected into an animal it causes antibodies to be formed in the injected animal's blood. If the antigen (egg-albumin) is reinjected into the animal thus prepared, a reaction takes place in the blood between the reinjected antigen and the antibodies prepared by the previous injection of the antigen. The presence of complement is, however, necessary. Further, as a result of this reaction between antigen, antibody and complement, the albumin molecule is broken down and a toxic product is formed known as anaphylatoxin. It will be readily seen that this theory agrees closely with the old views of the toxemias.

More recently a second theory has sprung up, and is seemingly growing steadily in favor, which opposes the humoral theory on the ground that the mere meeting of antigen and antibody in a complement containing medium does not adequately explain the symptomatology of anaphylactic shock, particularly the latent period of passive transmission.

According to Weil,[16] the humoral theory is committed to the belief that the circulating antibody may exercise either a protective or an injurious function whereas the cellular theory is strictly correlated with the view that the circulating antibody is invariably protective and the cellular antibody is invariably the agent of anaphylactic symptoms

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[15] Friedberger: Ztschr. f. Immunitätsf. **4**:218, 1910.

[16] Weil: J. Immunol. **1**:1, 19, 35, 47, 1916.

Cellular Theory.—Weil had previously stated that as a result of his study he had come to the conclusion that antigen and antibody could not coexist in the same field without union.

All writers agree that time is needed to produce the conditions necessary to anaphylactic shock. As Vaughan[17] expresses it: "If a reinjection of protein is made before a large amount of specific ferment is formed, no anaphylactic shock results. Anaphylactic shock is not to be feared if less than twelve days intervene between the first and second injections. Goodall[18] says that on an average a week or more is required for "incubation" between the primary sensitizating dose and the second activating dose.

Fordyce described the process of anaphylaxis as follows:

A foreign protein introduced into the organism causes an increase of antibodies for this protein. If after a so-called incubation period a second dose is given, the protein will be so rapidly disintegrated by the antibodies that toxic products are set free which give rise to the clinical phenomena. A further disintegration renders them harmless and the attack subsides.

Barduzzi says toxic substances that are formed in the blood or organic fluids act on the nerve cells. Urticaria is due to anaphylaxis. The symptoms are due to an irritation of the endothelium.

Rumpf found that the anaphylactic state persisted when the blood of a sensitized guinea-pig was removed and the blood of a normal animal substituted. Had the active agent of the anaphylactic phenomena resided in the blood desensitization should have ensued. Such was not the case, thereby proving that the reaction was cellular.

In brief, we may summarize the cellular theory, taking the facts from heterogeneous sources. A foreign protein is introduced into the organism. No symptoms follow. Antibodies are formed for the injected protein which are absorbed, anchored by the cells. Until enough antibodies have accumulated and have been anchored in the cells there will be no response to injections of the protein. Finally, however, the introduction of even a small dose of the sensitizing protein causes an explosion. "The reaction is an expression of the alteration of cellular equilibrium which results when external antigen is brought into contact with the cellular antibody" (Weil).

This theory is held by the proponents to answer all the objections raised against the humoral theory. It particularly explains the latent period of sensitization which the humoral theory could not. It is the period during which the process is gathering headway, when the cells are capturing and anchoring the antibodies as they are formed.

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17. Vaughan: Am. J. Med. Sc. **145**:161, 1913.
18. Goodall: Brit. J. Child. Dis. **9**:433, 1912.

The antibodies are so essential to the process of anaphylaxis that, naturally, much work has been expended in trying to demonstrate their presence.

Von Fenyvessy and Freund's [19] report of their studies is to the effect that the presence of antibodies in the circulation is not necessary to anaphylactic shock. As has already been shown in discussing other topics, this agrees with current opinion.

Perhaps one reason for lack of success in finding circulating antibodies lies in the results indicated by Hilda Hempl's [20] studies that in general a foreign serum disappears more quickly from the blood of an animal sensitized to that serum than from that of a normal animal, and that it disappears more quickly from the blood of a highly reacting animal than from that of a slightly reacting animal.

THE CUTANEOUS FOOD TEST

Schloss was among the first to demonstrate the possibilities of the cutaneous food test in cases of protein sensitization. Since that time the test has been developed widely both in use and in technic until today the average practitioner is as inclined to accept unquestioningly the apparent teachings of its results as he is to accept the results of the Wassermann test in syphilis. A brief study of the literature suggests that the circumstances surrounding the two are similar. Both tests lack full understanding. Both have their vagaries acting as they should not on the face of the evidence. Both are stronger on their positive than on their negative sides.

A few quotations will illustrate wherein the cutaneous food test is strong and wherein it is weak.

> The cutaneous food test may be taken as an index that the body cells have been brought into contact with a certain protein and that in addition to the production of the anaphylactic state antibodies of a protective and curative nature are produced. Cutaneous anaphylaxis cannot be accepted as a direct or reliable evidence of actual immunity any more than the agglutinins in the same capacity.[21]
>
> There is no experimental support for the theory that allergic skin reaction may be taken as an index to resistance and immunity insofar as it is possible to determine the presence of antibodies in vitro.[22]

Walker, writing on bronchial asthma, says that since many patients were sensitive to proteins of foods not eaten every day as well as to the foods eaten regularly, it is hard to say what part the less frequently eaten foods play. Furthermore, he continues, the fact that many of these patients have eczema as well as asthma complicates the interpretation of the positive skin test but does not detract from the value of the test. Speaking of the skin test as an index of desensitization, he says that usually the positiveness of the skin test decreases as the amount of protein in the treatment increases, provided the increase is slow and gradual. If the protein treatment is increased too rapidly, the skin test and desensitization cannot keep pace, so that eventually anaphylactic shock may result from the treatment.

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[19] Von Fenyvessy and Freund, J.: Ztsch. f. Immunitätsf. **22**:199, 1914.

[20] Hempl: J. Immunol. **2**:141, 1917.

[21] Kolmer and Berge: J. Immunology **1**:409, 1916.

[22] Kolmer: J. Immunol. **3**:10, 1918.

Walker implies, in explaining the failure of the skin test in two patients, that a hyperirritable skin may give unjustified results.

That the skin test is not always positive when it may clinically be expected to be is shown by Rackemann's figures. Skin tests were done in 127 cases. One or more tests were positive in seventy-four cases (50 per cent.) and of these seventy-four positive tests, forty (27 per cent. of the cases) were compatible with the patient's history. Rackemann insists that there must be agreement between the skin tests and the patient's history before the evidence of the skin test shall be accepted as conclusive.

BIOCHEMICAL INVESTIGATION

Not only have there been many attempts to solve the question of the nature of anaphylaxis on broad lines, but much work has also been done along special biochemical lines.

In 1913, Vaughan wrote that each protein molecule is composed of two groups, a primary or poisonous group and a secondary and characteristic group. According to Vaughan it is in this second group that proteins differ and in which their sensitizing properties lie.

Achard and Flandin [23] report that they have succeeded in isolating the poison formed during the anaphylactic state. They concluded that the poison is formed more abundantly in the nervous system than elsewhere; that it is probably a lipoid substance; that the subject is not always toxic to other animals of the species; and that its active anaphylactic properties are essentially heterogeneous and, particularly, homogeneous.

Kahn and McNeil [24] report that the specificity of the anaphylactic reaction depends on the chemical structure of the protein molecule and that if the molecule be split, its anaphylactic specificity is lost.

To this opinion as to the catabolic nature of the anaphylactic reaction Miller [25] adds his testimony. He says that two or more antigens may produce the same antibody and the same antigen may produce two or more antibodies. He explains that the relation of antigen to antibody does not depend on the entire protein molecule and it so happens that various unrelated substances contain these groups and so produce a common antibody.

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[23] Achard and Flandin: Compt. rend. Soc. de biol. **83**:25, 1912.

[24] Kahn and McNeil: J. Immunology **3**:277, 1918.

[25] Miller: J. Immunology **1**:383, 1916.

Obviously, if these statements are true, the explanation of such multiple sensitization by unrelated substances as seen in the second clinical case, and as has been so frequently encountered by others, may lie therein.

Jobling [26] stated in a discussion of anaphylaxis before the Society of Immunology that the lipoids, which some accuse of being actively concerned in the production of the phenomena of anaphylactic shock, can cause shock but are not able to sensitize. Wilson confirms the statement.

Saula says that there is a marked increase in soaps, fatty acids and lipoids subsequent to sensitization. He suggests that anaphylaxis may be due to increased saponification. Peterson and Jobling found that soaps injected intravenously into guinea-pigs in proper doses produce the symptoms and postmortem findings of anaphylaxis.

It has been asserted from time to time that kaolin broths, starch broths, guinea-pig serum after treatment with chloroform and ether and iodized guinea-pig serum were capable of causing anaphylactic shock and that their injection was an adequate method of studying the phenomena.

Loewit denies that these substances are capable of causing anaphylactic shock and that they furnish an adequate method of study. He finds that symptoms resulting from the kaolin and starch preparations are purely mechanical effects caused by large particles of the kaolin or starch being carried into the vessels by the injection and there producing thrombi. Likewise, the fatal effect of chloroform and ether serum is not due to anaphylaxis but to thrombi. True anaphylactic death Loewit says may occur in one of two forms—suffocation arising from bronchiospasm with secondary inflation of the lung or by peripheral or central paresis of the breathing apparatus with more or less edema and hyperemia of the lungs and more or less acute pulmonary dilation. The thoracic breathing always ceases before the abdominal.

Kleinschmidt [27] found that guinea-pigs can be sensitized per os by boiled or unboiled cow's milk and that the active factor was the milk albumin, the casein merely causing a condition of hypersensitiveness.

Weil says that in the guinea-pig anaphylactic death is due to a cellular reaction and that the serum changes play no part in it but, on the other hand, in prolonged or delayed shock in the dog striking alterations occur in the chemical composition of the blood. Weil has himself contributed largely to our knowledge of anaphylactic serums by his widespread researches. He states that immune serum consists of two substances, one thermolabile (precipitin), the second thermostabile (sensitizin). Heated precipitin will unite with the antigen but has lost its power of precipitating. It has lost its ergophore group and retained its haptophore. Moreover, Weil has found that precipitating serums which give a voluminous precipitate with certain concentrations of the antigen may fail to give any precipitate with still higher concentrations. This zone of absent precipitation he calls the prozone.

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[26] Jobling: J. Immunol. **1**:491, 1916.

[27] Kleinschmidt: Monatschr. f. Kinderh. **11**:664, 1913.

Disassociation of the precipitate, which probably occurs within the body, sets free antibody in a form which sensitizes passively but fails to give a precipitate reaction; but as has been stated in another place and connection, the antigen and precipitating antibody do not coexist in the same fluid without union.

The precipitate represents a complex of both factors, antigen and antibody; neither very largely destroys the other if, indeed, any destruction occurs. In this the anaphylactic process resembles the precipitation reaction in the test tube which is not accompained by the chemical destruction of either factor. It is immediate. It proceeds in the absence of complement. It requires relatively large amounts of antibody and relatively minute amounts of antigen.

This rapid survey of the field of protein sensitization is far from complete. Many articles have of necessity been passed over, many special researches omitted. Yet it is hoped that the broad lines have been drawn so fairly as to give an honest view of the field as a whole.

SUMMARY

1. Protein sensitization is now an accepted fact.
2. Theories as to its meaning and its mechanism differ.
3. Much that has been published concerning the process lacks confirmation.
4. Much work is still necessary in allied fields, such as the diatheses and the intoxications, before full use can be made of the new cult.
5. In the meantime while accepting the principles of the cutaneous food test, interpretation must await fuller, better defined understanding of the process of protein sensitization before it can attain its greatest efficiency.

PROTEIN SENSITIZATION IN SKIN DISEASES: URTICARIA AND ITS ALLIES *

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INTRODUCTION

One man's meat is another man's poison. This venerable aphorism attests the antiquity of our practical knowledge of sensitization. The first scientists to note the phenomenon with wonder were Jenner and Magendie. The first to note it appreciatively and reflectively was Richet.[1] The first to bring it into relation with cutaneous medicine were von Pirquet and Schick.[2] The only notable efforts to apply it to diagnosis were made by Smith [3] in connection with buckwheat poisoning, and by Schloss [4] in connection with egg albumin urticaria. The von Pirquet [5] test for tuberculosis suggested a method by which sensitization to various proteins could be clinically determined. Smith and Schloss, as stated, were the first to apply the procedure with results. In the meantime, White,[6] Strickler,[7] Blackfan,[8] McBride and Schorer [9] essayed in this field, but their investigations concerned chiefly eczema and, although their enthusiasm was compelling, the disease they mainly

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

1. Richet: Anaphylaxis; Bligh's Translation, London, University Press, 1913.

2. Von Pirquet and Schick: Die Serumkrankheit, Leipzig, 1905.

3. Smith: Arch. Int. Med. **3**:358, 1909.

4. Schloss: A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**: 341 (June) 1912.

5. Von Pirquet: Allergy, Arch. Int. Med. **7**:259 (Feb.) 1911; **7**:283 (March) 1911.

6. White, C. J.: Two Modern Methods to Be Employed in the Treatment of Chronic Eczema, J. A. M. A. **68**:81 (Jan. 13) 1917.

7. Strickler, A.: Anaphylactic Food Reactions in Skin Diseases, New York M. J. **104**:198 (July 29) 1916.

8. Blackfan: Cutaneous Reactions from Proteins in Eczema, Am. J. Dis. Child. **11**:441 (June) 1916.

9. McBride and Schorer: Erythematous and Urticarial Eruptions Resulting from Sensitization to Certain Foods, J. Cutan. Dis. **34**:70 (Feb.) 1916.

dealt with has no place in this paper, except where a liaison is established by factors common to the dermatitis and urticaria groups.

The similarity of serum sickness to urticaria is striking. Von Pirquet and Schick's work suggested that all urticaria was an anaphylactic manifestation. Osler's studies on the syndrome of toxic erythema, wheals, purpura and bronchial asthma in the later light of Richet's publications further substantiated the belief. The widely recognized fact that some foods, particularly strawberries, bivalves, and crustacea invariably provoked urticaria in certain persons, added to the growing edifice. In his case of buckwheat poisoning, Smith made percutaneous tests with the offending substance and produced local reactions. Schloss tested a patient with egg white urticaria in a like manner and with like results. The evidence for anaphylaxis seemed complete. Protein extracts of nearly all foods have been manufactured and percutaneous tests have been made with them. The purpose of this paper is to discuss whether, by means of this procedure, it is possible to detect the determining factor or factors in urticaria and kindred dermatoses.

Of fifty-three cases of urticaria, fifteen of which were chronic, studies were made in fourteen of the latter. Cases 7 and 11 were observed only as to their response to suprarenal extract. The other twelve were analyzed in this respect, as well as in relation to the cutaneous reactions. The time required for careful tests, their reading and interpretation, together with the difficulty of cooperation on the part of patients, precluded a more extensive series. Intensiveness of study is offered instead. As the work progressed, it rapidly became evident that the method was difficult to pursue and apply, and that it would offer but little to those in quest of a simple and direct means to isolate the cause or causes in individual cases of urticaria. There were numerous inconsistencies. It was not clear that allergy alone explained all cases. In short, the method proved either too much or too little, so that finally there took form in our minds certain questions. To answer these the work was and will be continued. Briefly, the problems appear to be as follows:

1. Are urticaria and allied conditions, notably angioneurotic edema, anaphylactic?
2. Do positive tests prove them to be anaphylactic?
3. If not, what may be their nature?
4. If not, what do the tests signify?
5. What is the practical value of the tests?
6. How are they to be clinically applied?

For purposes of reference, the cases studied are here recorded. Only the positive points have been noted, with a summary of its salient features after each history, and a short summing up of some general facts necessary for practical purposes. This paper aspires to avoid the onus of being of the case report type, but rather to outline what is known and to indicate what should be studied in connection with a most important dermatosis. Only positive reactions have been mentioned, but tests were made with all other foodstuffs consumed by the patient, and in certain instances with other substances, such as serum, epidermal substances, namely, feathers, hair, etc., and bacterial proteins.

REPORT OF CASES

Case 1.—Mr. L. A., aged 54, actor. Illness six months' duration. Sudden swelling of eyelids.

Diagnosis.—Angioneurotic edema. Supposed by patient to be due to light used in acting for screen pictures. He employed a "makeup" of a red and yellow grease paint and a brown powder.

Tests were made with the last two: red paint +++, yellow paint ++, powder —, cheese +++, coffee +++. Food tests made of substances ingested on day prior to last attack. In order to check up pathogenicity of positive substances, patient applied his make-up, and within an hour and a half his eyes began to smart and swell. Ingestion of suspected foods caused no reaction.

Therapy.—Suprarenal extract instillations in conjunctival sac to reduce swelling, and one hypodermic injection of 5 minims of this substance. Elimination of grease paint.

Result.—Cure.

Analysis.—Parenteral sensitization. Numerous positive responses checking up with suspected substances. Influence of suprarenal gland extract.

Case 2.—H. O. B., a man, aged 54, merchant. A seborrheal dermatitis of several years' duration. Several weeks sudden swelling of eyes. As a boy eggs and veal had caused headache.

Diagnosis.—Angioneurotic edema.

Tests.—Egg yolk +++, egg white —, pork +, tomato +, veal +++, walnut +.

Therapy.—Rigid diet. Suprarenal gland extract both in conjunctiva and hypodermatically.

Result.—No severe recurrence for seven months.

Analysis.—Numerous positive tests. Effect of suprarenal extract. Group reaction between walnut and egg (?). Cure by removal. (On an ocean journey patient ate egg and veal with immediate recurrence.)

Case 3.—D. K., a man, aged 66. Disease of four weeks' duration. Sudden swelling of eyes on Wednesday mornings; ate buckwheat cakes Tuesday evenings.

Diagnosis.—Angioneurotic edema.

Tests.—Buckwheat +++.

Therapy.—Suprarenal extract, conjunctival instillations. Elimination of buckwheat from diet.

Result.—Cure.

Analysis.—Single specific reaction. Elimination and cure.

Case 4.—Mrs. A. B., a woman, aged 65. Recurrent attacks of urticaria for three months. Indigestion and constipation for three years. Urticarial lesions associated with facial angioneurotic edema lasting from one to three days. The urticaria comes at 2 a. m., the angioneurotic edema toward evening.

Diagnosis.—Urticaria and angioneurotic edema.

Tests.—Beans ++, beet ++, cabbage ++, pork +, potato +, onions +++, oats, rice, rye, tomato, walnut + each. Confirmatory tests on cabbage and potato.

Therapy.—Cathartics, two colon irrigations; two suprarenal gland injections. Removal of positive foods.

Result.—Improvement within ten days. Very few wheals; no itching.

Analysis.—Intestinal derangement, numerous positive tests, influence of suprarenal extract. Possibly successive sensitizations. Improvement by removal of suspected foods.

Case 5.—Master M. C., aged 9; urticaria four years before. Annual recurrence; recent attack five days' duration. Associated by mother with eating of salmon. Marked constipation.

Diagnosis.—Urticaria.

Tests.—Salmon +; all other foods —. Salmon fed to child produced no attack.

Therapy.—Removal of salmon, but lesions had already begun to involute without treatment.

Result.—Spontaneous cure.

Analysis.—Abnormal digestion. Reacts to one food. This food apparently bears no causal relation to disease.

Case 6.—Mr. W. F., aged 29, merchant. Disease of five months' duration, beginning suddenly after attack of acute indigestion. Spleen and glands in general enlarged since childhood. Wassermann test, blood count and search for plasmodia, all negative.

Diagnosis.—Chronic urticaria.

Tests.—Beef +++, cabbage ++, casein +++, carrots +++ and ++++, cheese +++; corn ++; lamb +++; whole milk +++; veal +++; wheat glutein ++, wheat gliadin and globulin +. Patient noticed that his attacks were precipitated only by carrots when the suspected foods were eaten serially, experimentally to corroborate the cutaneous tests.

Therapy.—Colon irrigation without improvement. Suprarenal extract injection, 7 minims every five days, for five injections. Slight improvement. Elimination of suspected foods, particularly carrots.

Result.—Now without attacks for three months with only carrots removed from diet.

Analysis.—Successive sensitization. Group sensitization; specific. Offending food corroborated by diet. Treatment of digestive tract. Influence of suprarenal extract. Cure by removal of carrots.

Case 7.—Miss E. F., aged 21. Chronic urticaria six months' duration. Six minims suprarenal extract, complete relief at once. Well from January 25 to Aug. 6, 1917. Recurrence. Suprarenal extract injected August 6, 8 and 13. Well for two months. Not observed after this.

Analysis.—Effect of suprarenal extract.

Case 8.—Master M. K., aged 4½. Urticaria six months.

Tests.—Barley, beef, bluefish, wheat ++++ each; whole egg and rice + each.

Analysis.—Group reaction.

Case 9.—Mr. A. M. D., aged 22.

Diagnosis.—Recurrent urticaria for four years.

Tests.—Tomato ++++.

Therapy.—Elimination from diet of tomatoes.

Result.— Well in four days.

Analysis.—Single specific reaction. Cured by removal.

Case 10.—Mrs. C. M., aged 31. Ill for two years; constipated.

Diagnosis.—Urticaria.

Tests.—Cod, pork, corn, coffee and tea ++ each; coco, coffee, lamb, lettuce and wheat + each.

Therapy.—Elimination of suspected articles from diet, on Jan. 21, 1920. Well for a week. Recurrence, with symptoms of acute gastritis. Diet continued. Free from urticaria for another week. March 5 slight recurrence.

Result.—Improvement but no cure on diet modified according to tests.

Analysis.—See result; also indigestion. Sensitization to several proteins. Group reactions.

Case 11.—Mrs. H. N., aged 50. Urticaria for four weeks. One injection suprarenal extract; well for three years.

Analysis.—This case illustrates the use of suprarenal extract; the lesions vanished within five minutes after the injection.

Case 12.—Miss E. P., aged 18. Ill for two and a half months; constipated.

Diagnosis.—Urticaria.

Tests.—Lima beans ++++, wheat ++, beef, cheese, coffee, chicken, rice, rye + each.

Therapy.—Elimination of suspected foods; catharsis; suprarenal gland extract.

Result.—Remission for two days.

Analysis.—See result; effect of therapy; multiple reactions; group sensitization.

Case 13.—Mr. D. S., aged 70. Ill four months; constipated.

Diagnosis.—Urticaria.

Tests.—Lamb and potato +++, spinach +. Patient discontinued visits.

Therapy.—None instituted.

Analysis.—Multiple or group reactions. Collapse caused by suprarenal injection administered by previous physician.

Case 14.—Miss S. W., aged 9; ill for five years, nausea, chronic constipation.

Diagnosis.—Urticaria.

Tests.—Egg +, salmon ++. Discontinued visits.

Therapy.—None instituted.

Analysis.—Multiple reactions.

I. TECHNIC

1. *Substances and Methods Used.*—The commercial products of a large pharmaceutical firm were employed in the work. It may be assumed that these preparations are at least as conscientiously manufactured as the drugs on which physicians rely in their practice. Nevertheless, it is admitted that investigators should master the art of making their test substances themselves, as Wodehouse [10] did, in order

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10. Wodehouse and Olmstead: Preparation of Vegetable Proteins for Anaphylactic Tests, Boston M. & S. J. **176**:467 (March 29) 1917. Preparation of Animal Proteids for Anaphylactic Tests, Boston M. & S. J. **177**:85 (July 19) 1917.

to be able to vouch for every aspect of their experimentation. Should it ever be shown that the commercial proteins fall short in any respect, the work herein embodied is worthless. It is impracticable both for the patient and the observer to attempt more than twenty tests at a sitting. The skin is cleansed with ether, and a minute bloodless excoriation is produced at as many points along the forearm as tests are planned. A drop of decinormal sodium hydrate solution is deposited on each excoriation, and a small quantity of the protein is rubbed in with a fresh wooden applicator for each substance. Controls are made with the alkali. At first only one control was employed, but it was noted that the controls themselves vary, those near the elbow bend being larger than those near the wrist. Thus, we decided to place four controls at equal distances from the cubital fossa to the wrist in a row parallel to those of the test. If this is not done, accurate readings are impossible, all contrary statements notwithstanding, and it will be observed that the control lesions grow progressively smaller as the hand is approached.

2. *Vagaries in the Tests.*—It might be desirable to employ emulsions of raw foods for investigation. But these would spoil, and the entire literature indicates both that foods are not absorbed through the intestine in their original physical state, and that peptones and proteoses and their parent substances interreact specifically as anaphylatoxins. What is more important is that both tests and controls exhibit numerous vagaries. At times the latter exceed the former in intensity. At times responses occur to articles never ingested. This, in itself, however, has less meaning than might be imagined, but there are certain group reactions, as in Schloss' egg albumin case, that have a definite enough explanation. In urticaria, usually, there is dermographism, a phenomenon elicited in producing the excoriations.

3. *Reading the Tests.*—Thus, the reading of the tests introduces the personal equation, and yet the tests can be read with a reasonable degree of accuracy by allowing time for traumatic irritation to vanish, and by reading carefully against the controls. The reaction shows, within from ten to thirty minutes, the following features: a wheal and a stellate erythematous zone about it. If the wheal equals that of the control, and presents no erythema, it is negative, or at the most +—; if it is half again as large as the control, it is, + positive; if twice as large, ++; if three times as large +++; or if it is but half again as large and surrounded by erythema, it is ++, and so on. A wheal twice as large as the control, with a marked erythema, is +++; and everything over the above is ++++. Of course, these standards are largely subjective, and each investigator must evolve his own scale.

Tests vary slightly in intensity from time to time, but are rarely absolutely inconsistent for a given substance. Occasionally, this is not the case, and a test which at one time is positive and a week later negative, perhaps indicates the negative or antianaphylactic phase. At times, as in Case 13, the reaction may be delayed by as much as five hours, but even in this instance, correct readings, subsequently corroborated as above, were made within fifteen minutes. Strickler and Goldberg,[11] however, considered no test positive that did not persist for forty-eight hours. They, however, used the intracutaneous method which we have not attempted. Several patients reported later developments, and so far as the percutaneous tests go, Strickler's experiences do not hold.

II. IS THE SUBSTANCE THAT ELICITS A POSITIVE LOCAL REACTION A SPECIFIC PROVOKING CAUSE OF THE DISEASE?

1. *Specificity.*—The term specific, as applied in anaphylaxis, is a trifle confusing. A distinction must be made between biologic and chemical specificity. Anaphylatoxins that are biologically unlike may be chemically similar, and thus two proteins biologically distinct, may nevertheless call forth anaphylaxis. Richet stated that when we speak of specificity, it is because the preparatory substance always coexists with the exciting substance in the organic fluids we use (see section on apotoxin, and compare with Vaughan's[12] split proteins). This fact is nicely illustrated in Schloss' case which gave positive cutaneous reactions to various egg, almond and oat derivatives. Schloss was further able to show by cutaneous tests that, related to almond proteins, were those of peach, prune and plum kernels, strawberry, pear, apple and cherry seeds, but that grape and orange seeds were not related. Related to oat were rice, barley and rye, but corn and wheat were not, etc. The implication, obviously, is a chemical identity among these numerous substances. Thus, a person sensitized to a certain protein would respond to others in a kindred chemical group, although never actually sensitized by them, as is further shown in the studies of Wells and Osborn.[13] This fact is illustrated in nearly all of our own cases by the number of foods to which the skin

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[11] Strickler and Goldberg: Anaphylactic Food Reactions in Dermatology, J. A. M. A. **66**:249 (Jan. 22) 1916.

[12] Vaughan: Protein Split Products in Relation to Immunity and Disease, Philadelphia, Lea & Febiger, 1913.

[13] Wells and Osborn: Is the Specificity of the Anaphylactic Reaction Dependent on the Chemical Constitution of the Proteids, or on Their Biological Relations, Jour. Infect. Dis. **12**:341 (May) 1913; Wells: ibid. 455 (Oct.) 1908.

responds. In Case 2, a high degree of sensitization existed against egg yolk and veal. This is consistent with the extent to which these articles figured in the man's diet. On the other hand, there are instances in which only one substance appears to be the exciting agent, as in Smith's case of buckwheat susceptibility, and in Case 3 of our series.

2. *Nonspecificity.*—Multiplicity of reactions may be explained by chemical similarities in biologically totally unrelated substances. An episode early in this study that, by its apparent absurdity almost influenced us to discontinue our investigations, may be worth citing. An orthodox Jew gave reactions to pork, oysters and sturgeon, foods forbidden by the Mosaic law. This man may have transgressed as to his observances, or may have unknowingly partaken of the forbidden foods, but it is just as likely that the inconsistency had a biochemical basis.

3. *Chemical Specificity.*—It may therefore be reasonably concluded that the substance or substances eliciting positive local reactions are the specific pathogenic agents of the disease. Specific does not necessarily mean that only one food is responsible, but indicates chemical specificity in the sense that generically unrelated substances have a chemically identical architecture. This being true, the tests seem to be clearly specific.

III. CAN THE PHENOMENON BE ANAPHYLAXIS?

1. *Literature on the Subject and Present Views.*—From the preceding it may be inferred that urticaria and allied conditions may be caused by proteins in the sense that the offenders can often be determined by eliciting a local reaction, and that removal from the dietary of the indicated foods may be curative. We are definitely, then, dealing with food poisoning of some type. Is this type of poisoning anaphylaxis? To answer the question requires an outline of the nature of anaphylaxis. Richet's conception of this phenomenon is that a specific antibody is formed for each protein substance parenterally introduced. The union of antigen and its specific antibody forms a toxic entity which Richet designates as apotoxin. The nature of apotoxin is a matter of dispute, but perhaps Vaughan's assertion that it is a split protein radical is most commonly accepted. Clinically, anaphylaxis is exhibited by a series of explosive phenomena. Wolff-Eisner was the first to include among them urticaria, a concept soon substantiated by the writings of von Pirquet and Schick. The phenomenon depends on a preparatory invasion of the body by an alien protein, an incubation period, followed by a precipitating invasion of the identical protein, whereupon promptly occur a series of objective manifestations including pruritus, dyspnea, tachycardia, convulsions, bloody movements,

involuntary micturition, urticaria, diminished blood pressure due to bleeding into the sphlanchnics, and then either recovery or death. Richet first clearly observed and described the syndrome in connection with his work with actinaria, eel and horse serum. Since that time, intensive study has been accorded the subject, and a voluminous literature has amassed itself, but in no one particular are views yet quite in unison. So far as this paper is concerned, the authors feel incapable of critical review of the subject as anaphylactologists. What follows is an impersonal exposition of the minimum that must be discussed to develop the theme at hand in its clinical aspects.

2. *Similarity of Urticaria to Anaphylactic Skin Manifestations in Animals.*—Barnathon [14] describes anaphylactic accidents as characteristically sudden in appearance, and gradual in disappearance, subject to the laws of preparation and precipitation above described; as followed by a prolonged period of hypersusceptibility, and as due to albuminoids or their derivatives. Weil [15] considers the phenomenon due to a true antigen-antibody reaction. Bronfonbrenner's [16] views merit consideration, but are too technical to be included. Pick and Yamanouchi, as cited by Hektoen,[17] found a thermolabile substance the cause, and considered it an antigen. It could not be destroyed in six hours, at a temperature of 60 C., but lost its antigenic properties in fifteen minutes at 100 C. It resists drying, age and the addition of many chemicals and digestive enzymes, notably diastase, pancreatin, invertin and pepsin. The substance is always generically specific, except the lens, which sensitizes to lenses of all species but never to any other tissue. According to Rosenau and Anderson,[18] the amplitude of the sensitizing dose has nothing to do with prolonging the incubation period, but sensitization may persist for 732 days after the initial dose. Thus, from the literature, it follows that anaphylaxis is a state produced by introducing into an animal a foreign protein which so alters the body that when, within from ten to twenty days, a minute quantity of the same substance

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[14] Barnathon: De l'anaphylaxie alimentaire: etude clinique et experimentelle, Thèse de Paris, 1911, No. 185.

[15] Weil: Anaphylaxis and Its Relation to Problems of Human Disease, Lancet-Clinic, Nov. 19, 1913. On Antisensitization with Observations on Non-Specificity in Anaphylaxis, Ztschr. f. Immunitätsforsch., December, 1913.

[16] Bronfenbrenner: Specific Parenteral Digestion and Its Relation to the Phenomena of Immunity and Anaphylaxis, J. Lab. & Clin. Med. **1**:573 (April) 1916. The Nature of Anaphylatoxin, J. Exper. Med. **21**:480 (May) 1915.

[17] Hektoen: Allergy or Anaphylaxis in Experiment and Disease, J. A. M. A. **58**:1081 (April 13) 1912. Precipitation Production in Allergic Rabbits, J. Infect. Dis. **21**:279 (Sept.) 1917.

[18] Rosenau and Anderson: Further Studies on Anaphylaxis, Hyg. Lab. Bull. **45**: (June) 1908. Further Studies on the Phenomenon of Anaphylaxis, Hyg. Lab. Bull. **50**: (April) 1909.

is introduced, a definite syndrome is provoked. The underlying mechanism is not entirely understood, but depends on one factor or on a combination of the factors outlined. The body cells are altered to become most susceptible to a substance not inherently poisonous. The sensitization may persist for two years, as Rosenau and Anderson have shown, and the provoking substance is highly resistant to physical, chemical and digestive agents.

3. *Allergy, Idiosyncrasy, Susceptibility and Hypersusceptibility.*—After a body has been sensitized, its cells are temporarily or permanently altered in such a manner that they have become susceptible to formerly harmless proteins. In other words, their reactive powers have undergone a subtle metamorphosis. Pirquet designates this fact by the term allergy. Allergy indicates, practically, a cell hypersusceptibility to foreign proteins demonstrable by exposing the cells to small amounts of a sensitizing substance, whereupon a local, visible, inflammatory reaction arises. Pirquet called the local excitant allergen, and considered it analagous to Detre's antigen. Both in anaphylaxis and allergy periods develop in which, for reasons needing no elaboration at this point, sensitized organisms fail to respond to the precipitating substance. This phase of nonreactibility is called anergy. Antianaphylaxis is the state of desensitization.

In the preceding paragraph the word hypersusceptibility was employed. Hypersusceptibility, as Hektoen explains, is not synonymous with anaphylaxis. In a given animal a peculiar toxic reaction, depending on uniformity of the offending protein, is hypersusceptibility. In anaphylaxis, which is the result of sensitization, no matter what proteins are employed the symptoms are constant. Von Behring,[19] who noted anaphylaxis in horses against the bacillus of Nicolaier, and of various animals to diphtheria antitoxin, termed the phenomenon hypersusceptibility. This is untechnical usage in the modern sense. Anaphylaxis, then, is an artificial and restricted form of induced hypersusceptibility—a condition *sui generis*. Hypersusceptibility cannot be transmitted artificially to normal animals (it is a congenital characteristic), while anaphylaxis is transmissible. Idiosyncrasy is a broad and ill-defined term. It signifies an unusual body response to a substance. A person rendered restless by morphin, or one who gets an erythema from arsenic, has an idiosyncrasy to these substances. So, too, one who is nauseated by a given food without sensitization. Susceptibility signifies the normal tissue response to given substances, such as increased vascular tone, perhaps, to digitalis. Hypersusceptibility is an idiosyncrasy when not anaphylactic. When anaphylactic, if the word hypersusceptibility may be employed at all, it signifies an acquired characteristic due to artificially induced, definite body alterations. Hair splitting as these distinctions must seem, since in technical usage they have acquired definite significance, their definition must be understood.

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[19] Von Behring: Allgemeine Therapie der Infektionskrankheiten, Lehrbuch der Allgemeinen Therapie, Wien., 1899. Von Behring and Kitashima: Ueber Veminderung und Steigerung der ererbten Giftempfindlichkeit, Berl. klin. Wchnschr. **38**:157 (Feb. 11) 1901.

4. *Anergy.*—To revert to the question of anergy alluded to above: If a sensitized animal, as Besredka, Nicolle and Otto and numerous others have amply demonstrated, be reinjected before the incubation period is complete, anaphylaxis does not take place. Also, shortly after anaphylactic shock, if animals are reinjected, the phenomenon fails to appear. Thus, by injecting at too short intervals for anaphylactic manifestations to recur, the animal can be rendered immune. In other words, it has become desensitized, and it is widely accepted that immunity and anaphylaxis are one in mechanism and significance. The state after anaphylaxis which is free from reactability to the alien protein is what von Pirquet designated as anergy.

4. *Nonprotein Substances and Anaphylaxis.*—Curiously enough, substances not proteins are capable of producing a condition at least simulating anaphylaxis. It is too fresh in the minds of physicians to need emphasis that arsphenamin is one of these, as pointed out by Homer Swift. Adercco[20] found a similar state of affairs in animals in the experimental use of cocain. The possibility of cumulative effect, however, must not be overlooked. On the other hand, it is conceivable that chemicals may alter body proteins of the host in such a manner as to convert these, in effect, into alien proteins capable of producing anaphylaxis. No experimental evidence of this exists.

5. *Humeral and Cellular Theories.*—The final scene of the anaphylactic phenomenon is the cell, but it has not yet been positively decided whether the entire action takes place there, or whether its earlier phases occur in the body juices, subsequently to be transferred to the cell for the dénouement. Thus, two schools exist, one favoring the cellular, the other the humeral theory. There is a third which records the entire process as physical. We do not pose as arbiters in the debate. As a matter of fact, so far as our theme is concerned, it makes no difference which view is academically correct, for in the final analysis, it is the cell that is affected.

6. *Clinical Mechanism of Sensitization: The Portal of Entry Intestinal.*—Thus far, mainly abstract questions of anapyhlaxis have been discussed. If urticaria is an anaphylactic phenomenon due to food sensitization, the question arises whether alimentary sensitization can

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[20] Adercco, V.: Action plus intense de a cocaine quand on en répète l'administration a courte intervalle. Arch. Ital. de Biol. **20**:32, 1896.

take place. Normally, only amino acids permeate the intestinal wall; peptones and proteoses do not. Amino acids cannot cause anaphylaxis. Peptones and proteoses can, and they react biologically specifically with their parent substances, or chemically specifically with related substances, as brought out in Schloss' work. Thus, it is necessary to inquire whether peptones and proteoses ever enter the circulation through the intestine. If they do, can they accomplish this through a normal intestine, or must there be an organic or functional derangement to permit this? Obviously, foods in their original chemical state are rarely assimilated. For such absorption, however, the proteins must be in solution, or at least partly hydrolyzed. Hektoen states that sensitization has been experimentally produced in guinea-pigs by the "inhalation of a fine spray of foreign serum." It is possible that some of the inhaled protein may have reached the stomach; it is also likely that some inhaled pollens reach the stomach in asthmatics and in victims of hay fever. But the supposition generally held in the latter conditions is that the protein is absorbed through the bronchial mucosa. Since there are no ferments in the latter, we may assume, with reason, that the protein is absorbed in its natural state. The inference, as it relates to the gastro-intestinal mucosa, is obvious. Furthermore, sensitization can be accomplished by rectal injection in animals, indicating absorption of unchanged protein through the alimentary mucosa.

Barnathon has exhaustively analyzed these considerations. He points out, assuming the possibility of intestinal sensitization, that patients presenting the condition are habitually troubled with constipation, or enteritis, or enterocolitis or diarrhea, and that even small amounts of precipitating doses enterally absorbed, cause the phenomenon precisely as in experimental parenteral anaphylaxis. He was able to cure urticaria in a young woman whose attacks were caused by shell fish and accompanied by vomiting and diarrhea, when he prescribed pepsin and hydrochloric acid for her achlorhydria. Arthus, cited by Barnathon, introduced antigen rectally into a rabbit, and seventeen days later elicited anaphylaxis by injection. Bouteil[21] injected the preparatory dose into the portal and mesenteric veins of dogs and rabbits, and produced anaphylaxis after a suitable incubation period. Nobecourt[22] sensitized rabbits to egg white by gastric and rectal injection. Barnathon concluded that alimentary sensitization could occur and was due to absorption of proteins incompletely hydrolyzed because of some disturbance of the digestive juices. In dogs, previously sensitized to egg white, he was unable to obtain toxic effects

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21. Bouteil: Des voies d'introduction des substances anaphylactisantes, Thèse de Paris, 1910.

22. Nobecourt, P.: Mortalité des lapins sounis a des injections de blanc d'oeuf, Compt. rend. Soc. biol. **66**:850, 1909.

by injecting that substance, digested for forty-eight hours by pancreatin in an incubator. Van Alstyne,[23] experimenting with dogs, proved that egg albumin introduced into the stomach or intestine (except the duodenum) passed into the blood. With proper controls, she obtained anaphylactic shock with a dog's blood (so prepared) in guinea-pigs sensitized to albumin. She duplicated these results by feeding egg white by gavage, thus not injuring the alimentary tract. In her first series of experiments she had ligated the intestine to form a cul de sac. With milk, and horse and beef serum she reproduced both series of experiments. Ligation of the duodenum gave no consistent findings, nor did edestin give consistent results. She concluded that protein was absorbable unaltered through intact alimentary epithelium, but that trauma favored the phenomenon. She decided that conditions interfering with digestion increase absorption of unaltered protein, and applied her views particularly to urticaria. Ganghofer and Langer [24] showed that in animals under eight days old, in massive doses, the gut was permeable to alien proteins, and in two debilitated infants undigested egg white was demonstrated in the blood by precipitation tests. In this connection, be it particularly noted for future reference, that Cannon [25] observed that the alimentary canal is highly adaptable in its function. Experimentally he found that the saliva of dogs feeding on a rich carbohydrate diet acquired marked amylolitic powers, and that animals, when enraged, showed diminished intestinal peristalsis.

Uhlenhuth [26] found that prolonged feeding of egg to rabbits produced specific precipitins in their blood, and Ascoli [27] was able under the conditions mentioned to determine its presence in the blood within three quarters of an hour after ingestion. Vaughan, Cummings and McGlumpy [28] demonstrated by anaphylactic tests, that rabbits absorb incompletely digested protein through the alimentary tract. Schloss and Worthen,[27] by applying the facts recited, determined that such substances appeared in the urine. In normal infants they found that imperfectly digested proteins were absent from the urine, but were present in infants with gastro-intestinal disturbances which evidently favored assimilation of incompletely digested proteins.

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[23] Van Alstyne, E. V.: The Absorption of Protein without Digestion, Arch. Int. Med. **12**:372 (Oct.) 1913.

[24] Ganghofer and Langer: Ueber die Resorption genuiner Eiweisskorper im Magendarmkanal Neugeborener Tiere und Säuglinge, München. med. Wchnschr. **51**:1497, 1904.

[25] Cannon, W. B.: Recent Advances in the Physiology of the Digestive Organs, Am. J. Med. Sc. **131**:563 (April) 1906.

[26] Uhlenhuth: Neue Beiträge zur Spezifischen Nachweiss von Eierweiss auf biologischem Wege, Deutsch. med. Wchnschr. **26**:734, 1900.

[27] Ascoli in Schloss and Worthen: The Permeability of the Gastro-Intestinal Tract of Infants to Undigested Protein. Am. J. Dis. Child. **11**:342 (May) 1916.

[28] Vaughan, Cummings and McGlumpy: The Parenteral Introduction of Proteids, Ztschr. f. Immunitätsforsch. **9**:16, 1911.

As to clinical medicine, the practical inferences to be drawn from the statements made above are numerous. The intact intestine, as shown by Van Alstyne, may be capable of assimilating unaltered protein, and as shown by Arthus, is capable of assimilating altered protein. Abnormal intestinal mucosa, as indicated by Barnathon, is capable of this, and he includes in his conception of disturbances, those which are functional as well as anatomic. Bouteil's findings confirm this, as do those of all other authors cited. Schloss and Worthen, by their studies of infants, bring the work on animals into relation with human problems of sensitization, and Van Alstyne specifically applies her results to urticaria. It is perhaps speculative to remark here that the flora of the intestine, biliary disturbances, the free consumption of alcohol, spices and acid substances, may so influence the alimentary mucosa as to alter its permeability, or so influence the function of digestion as to alter the character of the proteins. By either means, or a combination of them, sensitization is as likely to occur in human beings as in animals. Herein lies probable clinical substantiation of experimental evidence. In this connection, emotional and nervous instability or strain may, in man, produce the digestive disturbances mentioned by Cannon as occurring in animals. Thus, may be accounted for practically the frequent occurrence of urticaria in neurotic and vagotonic persons.

So far as it is possible to translate human statements and physical signs into terms of morbid biology, with special reference to sound clinical medicine, many of our patients present features consonant with the ideas expressed in the foregoing paragraphs. Intestinal disturbances occurred in Cases 4, 5, 6, 10, 12, 13 and 14, a total of seven in fourteen. As a rule, the complaint was constipation. At times, nausea, vomiting, or diarrhea were found. In a woman, not included in this series, mucous colitis had existed for ten years, and the urticarial attacks began with vomiting.

7. *Clinical Mechanism of Sensitization: The Portal of Entry Parenteral.*—In experimental anaphylaxis it has been shown that the portal of entry may be either enteral or parenteral, and in human anaphylaxis it is clear that, when not artificially produced, as by serum injections, it is mainly enteral. Can it be parenteral? Pirquet and Schick state that guinea-pigs may be sensitized by inhaling sprayed foreign serum. In Schloss' patient, mere contact of egg with the lip produced urticaria. It is conceivable, however, that substances entering the mouth might have to be swallowed before being absorbed. In this connection it may

be remarked that such small amounts of alien protein may sensitize (1/1000,000 gm. egg white; Wells working with guinea-pigs), that sensitization through injured integument is conceivable. This entire question has not yet been adequately investigated.

If Case 1 of our series actually is an example of allergy, sensitization must have been parenteral, for the offending substances had been applied mainly to his eyelids. These substances gave positive local reactions percutaneously, and when, for purposes of corroboration, he applied the pigments to his lids, itching, burning, and slight swelling appeared within an hour and a half. Nothing is known of sensitization through normal integument, but it is possible that the skin at these sites always presents microscopic injuries, particularly in people applying cosmetics. This patient will receive further study.

8. *Clinical Mechanism of Sensitization: Hereditary, Congenital and Spontaneous Occurrence; Transmission Through Maternal Milk.*—Longcope [29] believes that hypersusceptibility is hereditary and at times spontaneous. Pirquet has shown that it may be congenital, for it is found in the offspring of anaphylactic animals shortly after birth. This, however, is merely an example of passive sensitization. Barnathon cites Hutinel's [30] observation of sensitization transmitted passively through human milk to nursing infants. The concept of hereditary anaphylaxis is difficult to grasp, unless acquired characteristics are transmissible. If the peculiarity was congenital in the first generation, it could be transmitted via the chromosomes, but this would be an example of hereditary transmission of a congenital variation, a concept conforming to our knowledge of the laws of heredity. If congenital in the first generation, and not acquired, the phenomenon would not be anaphylaxis, but hypersusceptibility or idiosyncrasy; for, having started spontaneously, it could not be construed strictly as anaphylaxis. Transmission of sensitization to offspring, or through the milk, are sound examples of the passive form, but are transitory, and the former variety has nothing to do with heredity.

9. *Influence of Drugs and Chemicals on Anaphylaxis.*—Banzhaf [31] and Steinhardt have shown that chloral inhibits anaphylactic shock, while lecethin does not. Stokes pointed out the value of atropin as a prophylactic in acute arsphenamin reactions, particularly of the type designated anaphylactoid by Swift. It is, of course, not quite clear how arsenic can cause anaphylaxis, but a discussion of this problem appears in an earlier passage (III, 4), and need not be repeated. The

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29. Longcope: Susceptibility of Man to Foreign Proteids, Am. J. Med. Sc. **152**:625 (Nov.) 1916.

30. Hutinel: Intolérance pour le Lait, La Clinique, April, 1908.

31. Banzhaf and Steinhardt: Vaughan's Split Products and Unbroken Proteins: A Comparative Study of Their Effects, J. Med. Res. **23**:5, 1910.

usefulness of suprarenal extract in inhibiting anaphylaxis is widely known, and will again be alluded to in an entirely different phase, particularly in its special application to urticaria. As Sâmberger[32] points out, the wheal is primarily due to a dilatation of vessels, and suprarenal extract narrows them. The chemical mechanism of this will be further explained later. Undeniably, suprarenal gland extract usually limits individual outbreaks of wheals, and at times controls urticaria completely. In our experience, the calcium salts are utterly valueless.

Suprarenal gland extract is most efficacious when employed hypodermatically. Its administration by mouth seems futile, for it does not survive alimentary digestion as an efficacious substance. In employing it, the possibility of cardiac collapse must be remembered, and if results are not obtained after one or two injections, they will not be obtained. H. Miller's suspension in olive oil is less toxic and seems no less efficacious than aqueous solutions. Its absorption is more gradual, and hence smaller amounts of the drug may be employed, with practically no risk to the heart. Instillation into the conjunctival sac promptly reduces the swelling of the eyelids in angioneurotic edema of these organs. This was observed in Cases 1, 2 and 3 of our series. In Cases 4, 6, 7, 10, 11 and 12, it was used with uniformly good results. In Cases 5, 8, 9, 13 and 14, it was not employed, either because of the youth of the patient, or because our studies had not sufficiently advanced, or, as in Case 13, because the drug was known to act badly. The patient in this instance, a man of 70, had been given an injection of the gland extract by another physician and had collapsed. Cases 7 and 11 were included in our series to illustrate the effect of the drug. The patient in Case 7 was a young woman whose first relief in six months immediately followed an injection. She remained well thereafter, as the history shows, for seven months. The second patient was a woman of about 50 who, after constant urticaria for four weeks, was cured within ten minutes of her injection, and has since remained well for a period of three years. Knowing that suprarenal gland extract curbs anaphylaxis, and that it often curbs urticaria, have we here evidence that urticaria is an anaphylactic phenomenon? Have we here the elements of axiom one? Have we a syllogism or a sophism?

10. *The Nature of the Anaphylatoxin.*—Proteins in their original state as ingested may be anaphylatoxic, and furthermore, parent substances react specifically with their derivatives, as repeatedly stated. What, then, are these products? Magendie noted the egg phenomenon in 1839, but could not explain it. Rosenau and Anderson, working

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[32] Samberger: Die Entzündliche und Urtikarielle Hautreaktion, Dermat. Wchnschr. **61**:739 (July) 1915. Weitere Erfahrungen über die lymphatische Hautreaktion, Dermat. Wchnschr. **65**:623, 1917.

with horse serum, noted that its toxic properties disappeared when heated at 100 C. for an hour, but could not confirm Besredka's observations that this substance lost its sensitizing properties through age. Fleischmann[33] digested beef serum with trypsin until the Biuret test failed. Such serum loses its precipitins, and this was further substantiated by Moreschi, Neisser and Sachs by means of the Bordet-Gengou test. However, in the course of digestion, preceding the loss of the Biuret reaction, substances capable of producing anaphylaxis exist. Werbitski[34] thus was able to elicit shock in guinea-pigs sensitized to serum by reinjecting peptones derived from like serum by digestion. Richet corroborates this in the statement "as long as the albuminoid molecule is not completely destroyed, even when it is broken up by tryptic digestion, it remains capable of producing anaphylaxis." Zunz[35] proved that primary proteoses could cause both active and passive anaphylaxis, but not thio-albuminose, or other so-called proteoses, Siegfried's pepsin, fibrin, peptone-beta, or any abiuret products of peptic, tryptic or ereptic digestion. Animals sensitized to hetero-proteose, protoproteose or synalbuminose (the primary proteoses) develop anaphylactic shock on reinjection with the original serum, hetero-albuminose or proto-albuminose. This does not occur with synalbuminose, thio-albuminose, or any abiuret products of any form of digestion. Hetero-albuminose and proto-albuminose sensitize and precipitate anaphylactic shock, while synalbuminose only sensitizes. It follows, therefore, that sensitization and the production of anaphylactic shock are due to different groups in the protein molecule. Pirquet long before, in the early days of anaphylaxis, stated that not all albuminoids were allergens, but that peptones acted weakly and leucin and tyrosin not at all.

Thus original proteins and their digestive derivatives, up to a certain point, are admittedly capable of intersubstitution, in the anaphylactic sense. After a certain point in cleavage, however, this no longer obtains. Moreschi, Neisser and Sachs, as quoted by Fleischmann, proved that amino acids could not be antigens. Pirquet's observations as to leucin and tyrosin apply here, as do Zunz's regarding any protein cleavage products beyond the biuret stage. Barnathon states that proteins of advanced decomposition, particularly leucin and tyrosin, do not cause anaphylaxis. Schloss and Worthen say "it has

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33. Fleischmann: Ueber die Prazipitogens Eigenschaft trypsinverdaute Rinderserum. Ztschr. f. klin. Med. **59**:515, 1906.

34. Werbitski: Contribution à l'étude de l'anaphylaxie, Compt. rend. Soc. de biol. **66**:1084, 1909.

35. Zunz: Contribution a l'étude de la digestion et de la resorption des proteins dans l'estomac et l'intestin grêle chez le chien, Mém Curonnés **20**:3, 1908.

been demonstrated that specificity is lost in protein cleavage products lower than the peptones." Saunders[36] implies all of the foregoing with regard to the effect of egg albumin and milk.

Thus sensitization is produced by proteins down to, but exclusive of, the amino acid stage. The conception depends on two factors as illustrated in the split protein conception of Vaughan, Zunz and others. According to Hektoen, in sensitization, bodies of the general nature of amboceptors are formed which are specific, and after uniting with complement and antigen, produce anaphylactic symptoms and lesions. This action depends on protein digestion, as seen after the injection of Witte's peptone, a split protein. Vaughan thinks a ferment exists in the organs of sensitized animals, capable of splitting protein. Bruck's[37] experiment practically substantiates all of this. He passively sensitized a guinea-pig with human serum of a person reacting to pork and produced anaphylaxis by a second injection of hog's serum.

Anaphylatoxins are proteins capable of withstanding heat of 100 C. for an hour, or peptones, or proteoses derived from these, or split proteins such as Witte's peptone. But no protein derivatives are among these that no longer give the Biuret reaction. The parent substances, and their derivatives, obtained by any type of digestion whatever, or chemical splitting, interplay in producing sensitization or precipitation, and are capable of provoking active or passive anaphylaxis. One element of the split protein acts generically, and the other specifically, and so far as the body is concerned it is conceivable, as Vaughan states, that in the last analysis anaphylaxis depends on protein-splitting ferments in the sensitized body.

11. *Demonstration of Sensitization by Local Reactions.*—Schloss' case of egg albumin urticaria, Wolff-Eisner's impression of this disease, Smith's case of buckwheat poisoning, amply illustrate the fact that allergy exists in the tissues of sensitized persons. These authors further show that it is demonstrable by local tests. As Vaughan indicates, the higher mechanism of immunity and anaphylaxis are identical, and in a similar fashion it is clear that all nutrition and immunity being in the same category, sensitization must bear a relation to nutrition equivalent to its relation to immunity. The curious fact remains that since urticaria is anaphylactic, local reactions may be elicited by so many substances in each case. This is explained by facts outlined earlier. In the first place, a person may be actually sensitized to more than one food, just as an animal may experimentally be sensitized to several substances. Second, specificity is chemical, as well as biologic,

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[36] Saunders: Serum Disease as a Clinical Manifestation of Anaphylaxis, Interstate M. J. **15**:576, 1908.

[37] Bruck: Experimentelle Beiträge zur Aetiologie und Pathogenese der Urticaria, Arch. Dermat. u. Syph. **96**:241, 1909.

and proteins fall into related groups as has been shown by Schloss (II, 1) and as follows from the studies of Banzhof and Steinhardt. As a matter of fact, in our series, Cases 2, 4, 6, 8, 9, 10, 12 and 13 responded to several proteins, but always with greater intensity to two, as in Case 2 (egg yolk and veal), or only one, as in Case 4 (onions), Case 6 (carrots), Case 9 (tomato), and Case 12 (lima beans). Case 8 responded intensely to barley, beef, bluefish and wheat. It will be a problem of the future to try to work out these group relationships in anaphylaxis, as only such a solution will increase the clinical value of cutaneous tests.

Perhaps the greatest practical light is thrown on multiple reactions and chemical and biologic specificity by the work of Wells and Osborn. These writers found that wheat and rye interreacted. Zein (corn) does not react to wheat gliadin, while hordein (barley) does. They continue:

> The specificity of the anaphylaxis reaction is determined by the chemical structure of the reacting proteins, rather than by their biological origin. The most reasonable explanation of these results is that both gliadin and glutein contain common groups which react with one another, and that the specificity of the anaphylaxis reaction is not dependent on the chemical makeup of the entire protein molecule.

Hordein reacts with gliadin, gliadin with glutein, but glutein does not react with hordein. Thus, probably, glutein and gliadin contain common groups. "Animals sensitized with proteins will, as is well known, react with either, and after recovery from reaction to one protein, the reaction given with the second protein is less severe."

12. *Summary.*—Different animals, as shown by Richet, present varying syndromes under anaphylactic shock, each species always presenting the same symptoms, whatever the protein used. Among symptoms of anaphylaxis in human beings, as shown by the writings of Schloss, White, McBride and Schorer, Wolff-Eisner, Pirquet and Schick, and others, may be included urticaria. Even in lower animals cutaneous manifestations, such as pruritus, occur. Anaphylaxis produces changed tissue reactions, or allergy, in the sense of Pirquet. Thus the skin may reasonably be included among the allergic tissues. It is compatible with our knowledge that sensitization may occur enterally, as well as parenterally, and thus, in human beings, incomplete products of protein cleavage may be absorbed by an abnormal intestine and sensitize the person. Sensitization of this sort is subject to the same laws as is the parenteral variety; namely, incubation, precipitation and desensitization after the shock. Even active and passive sensitization (Bruck) can be demonstrated by the serums of anaphylactic people, by means of the milk of sensitized women. The anaphylatoxin has distinct physical properties, and is both biologically and chemically

specific, the latter specificity being clinically as important as the former. It follows, since the skin is allergic, and since urticaria in general is an allergic phenomenon, that urticaria is probably an anaphylactic manifestation.

DO POSITIVE SKIN TESTS PROVE THAT URTICARIA IS ALWAYS ANAPHYLACTIC?

It is admitted that urticaria may be an anaphylactic manifestation, and that sensitization is demonstrable by local reactions or tests. Does it follow from this that positive tests prove that urticaria always is due to allergy? To discuss this we must take up several questions. 1. What is the nature of urticaria clinically, pathologically and pathogenically? 2. Is there anything in these conditions indicating anaphylaxis? 3. What is the nature of tissue reactions in general to pathogenic agents?

1. *The Nature of Urticaria Clinically, Pathologically and Pathogenically.*—Urticaria is an acute or chronic dermatosis characterized by the sudden appearance in crops of wheals. The duration of the disease may be indefinite, although the individual wheals are usually evanescent. Chronic varieties in which papules form are known and are related to prurigo. Bullous varities are related to Duhring's disease. The two last have been interpreted by Johnston and Schwartz [38] as anaphylactic manifestations. There is no substantiation of the belief. More important is the relation of urticaria to toxic dermatoses caused by drugs, unascertained factors, or appearing in general infectious diseases. The last might well be anaphylactic and of bacterial origin, but equally well might be more like drug eruptions and due to bacterial or metabolic toxins. The relationship of toxic rashes, purpura and erythema multiforme to anaphylaxis is strongly suggested in Osler's studies. An analogy between urticaria and hay fever is strikingly indicated in the writings of Robert Cooke and I. Chandler Walker, and a common bond between hay fever and urticaria is the asthma emphasized in Osler's group of diseases. That angioneurotic edema and urticaria are allied is clear from the frequency with which the former appears as a participant in the latter.

Pathologically, urticaria narrows itself down to an understanding of the wheal. Brun,[39] with egg albumin and milk, produced swellings in the ears of sensitized rabbits. True, they were not wheals, but such lesions do not develop in these animals. Undoubtedly, Schloss, Smith, Pirquet and Schick, and Longcope produced wheals locally by trauma, and the application of suitable protein in poisoning by egg albumin, buckwheat and serum. Thus in urticaria, specific wheals can be produced by specific toxins. On the other hand, dermographism exists nonspecifically in urticaria, and thus excoriations alone may excite wheals. It is for this reason that specific are compared with nonspecific wheals, as controls, in making and reading the tests.

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[38] Schwartz: Studies in the Metabolism of Dermatitis Herpetiformis, J. Cutan. Dis. **31**:994 (Dec.) 1913.

[39] Brun: Contribution a l'étude de l'anaphylaxie, Thèse de Montpellier **81**: 1905.

According to Kreibich,[40] wheals are due to the irritation of sympathetic cells through sensory irritants. The sympathetic ganglions are not diseased, but pathologically overfunctionate. He quotes Török[41] and Philipson, however, who considered wheals the result of toxins, and Quincke's edema is included in his generalization. More important than Kreibich's views are those of Sâmberger. He agrees with Török and Philipson to some extent, and also with Kreibich, but believes that a vasodilatation alone can produce no inflammation. Bier[42] amputated a hog's leg below a tourniquet. After removing the latter, and in spite of free hemorrhage, there was hyperemia. The explanations of Török, Kreibich and the Unna school would be inadequate to a situation in which hyperemia existed where there was a free flow of blood, as from the cut surface of the hog's amputation stump. Sâmberger, himself, thinks that the cells in the involved area have been asphyxiated, and that their oxygen hunger calls for an increased blood supply (hence, hyperemia) in order to bring more oxygen to the asphyxiated cells. Thus he concludes that capillary dilatation has this purpose. In addition, leukocytes bring nourishment to affected cells, and favoring this function is the lowered circulatory rate in hyperemia. These phenomena determine the first step in exudation, and an exudate shows the local need of cells for nutrition. In health, enough oxygen and nourishment are derived from the normally circulating blood. Exudation determines a hypersecretion of vascular endothelium, notably that of the lymphatics; and the endothelial cells, which are capable of an ameboid movement, locate themselves near disturbed tissue cells that require more oxygen and nourishment.

Hyperemia of the skin is observed in injuries by the sun, heat, mechanical agents and toxins, not through their direct influence on vasodilators, but because they thus subserve the increased need of the exposed cells for oxygen and nourishment. He regards urticaria in this category and explains the wheal on this basis. The edema of the collagen is caused by dilatation of the lymph spaces, and the wheal is not an angioneurosis but the result of an endothelial proliferation dependent on an attempt to oxygenate and feed asphyxiated and starving cells. The presence of mast cells proves this, and a wheal represents a compensatory hypertrophy of tissue and an increase of function designed to satisfy an imperative local need. He characterizes the wheal as a "secretory anomaly of lymph" or what he calls "a lymphatic hypersecretory efflorescence." He makes his classification more extensive than this paper requires, even including therein pemphigus. He distinguishes between ordinary and urticarial inflammation, stating that the same cause may incite in one person the former, and in another the latter, and that this rule applies to all injurious substances and traumas.

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[40] Kreibich: Die Angioneurotische Entzündung, Wien., 1905.

[41] Török and Hari: Experimentelle Untersuchungen über die Pathogenese der Urticaria, Arch. f. Dermat. u. Syph. **65**:21, 1903.

[42] Bier: Mares Physiology, Part 3, Division 2.

In his second paper he continues with the idea that the angioneurotic reaction, better called the "lymphatic skin reaction," is primarily due to anaphylaxis. He analyzes, in case reports, the relation between urticaria, diarrheas, weakness and asthma and discusses the rôle of vagotonia and sympathetic disturbances to the disease. Thus, he allies the mechanism to the ductless gland system. He calls anaphylaxis vagotonia acutissima, and serum sickness vagotonia acuta. In this sense he regards urticaria as an endocrine disease in which the vagus dominates the sympathetic system. In the final analysis anaphylaxis causes local asphyxia and malnutrition; wherefore, hyperemia, exudation and an endothelial hyperplasia develop. In other words, because of sympathetic paralysis as artificially produced by Claude Bernard, who elicited sympathetic ischemia by extirpating the cervical gland, the blood is locally squeezed out of the tissue in urticaria. Hence, an increased demand for oxygen is registered in the form of a final hyperemia and wheal formation. Administration of suprarenal gland extract in urticaria cured several of Sâmberger's cases. Gradinescu extirpated suprarenal glands in animals and found that the lymph flow from the thoracic duct was increased. Sâmberger thus concludes that since suprarenal extract increases the circulatory rate by narrowing the capillaries, it prevents anaphylaxis, and causes involution of wheals by the resultant increase of oxygen content in the asphyxiated cells.

Sâmberger's theory may be overnice, but it is so far in conformity with experience that his objective observations are correct. The wheal is due to the exudation. The mast cells definitely indicate the need for hypernutrition. The collagen is swollen. Suprarenal gland extract causes the wheals to involute. Whether the entire process depends on asphyxia or not, we cannot state, but whatever Sâmberger's explanation, there is something fundamental in his concept.

2. *Indication of Anaphylaxis.*—Consensus of opinion favors the belief that suprarenal gland extract inhibits anaphylactic shock. Its place in urticaria is established beyond doubt. Does this indicate that urticaria is anaphylactic? Sâmberger holds that any agent, physical, chemical, or toxic, can produce cell asphyxia, that cell asphyxia determines the wheal, and that the wheal disappears when oxygenation is

re-established, as by the effect of suprarenal gland extract. If these views are correct, wheals can be produced otherwise than in anaphylaxis, an suprarenal gland extract, because of its utility in urticaria, would not necessarily prove that the latter is anaphylactic. The effect of suprarenal gland extract in our cases, both of angioneurotic edema and urticaria, has been recorded (III, 9).

Unquestionably dermatitis venenata, some forms of which have groundlessly been considered anaphylactic, does not respond to suprarenal gland extract. Neither do these forms give positive cutaneous reactions, and nevertheless, some confusion exists as to this group. Urticarial elements, small lesions suggesting wheals, have been seen in all types of acute dermatitis. Urticarial lesions have been described in syphilis, particularly by Hazen and Sutton, and nevertheless no percutaneous responses exist in this disease; nor does suprarenal extract cause their involution. Wechselmann thought his case of satinwood dermatitis anaphylactic. The urticaria caused by the nettles is apparently not anaphylactic, and the exciting agent in primrose dermatitis, as shown by Simpson, is not a protein. In short, syphilis, nettle, primrose, rhus, and other forms of dermatitis venenata may have urticarial lesions, but these are not anaphylactic in causation. They do not respond to suprarenal gland substance, and, so far as our experience goes, no type of urticarial lesions, except those of presumably anaphylactic origin, give cutaneous reactions, or respond to suprarenal extract.

3. *Nature of Tissue Reactions in General to Pathogenic Agents.*—Whereas, in general, urticaria is perhaps justifiably considered anaphylactic, it is reasonable to suppose that other pathogenic agents, as shown above, may cause similar tissue responses. It has already been noted that wheals at times are seen in syphilis and various forms of acute dermatitis of known and unknown causation. Thus the wheal alone does not indicate anaphylaxis. On the other hand, a dermatosis characterized by wheals and giving a percutaneous protein reaction may be reasonably certainly regarded as anaphylactic, for such reactions are not encountered save in diseases due to sensitization. No toxin of any sort, of itself, causes disease. Disease is just as much a matter of tissue response, as of a pathogenic agent, and depends on an interplay of the two. Thus, no disease can arise without tissue hypersusceptibility. In this sense there is nothing peculiar about urticaria; but it is peculiar to urticaria that the special mechanism is one of general sensitization, a condition registered in given cells as allergy which can be demonstrated by a special test, not known except as to allergy. In other words, in urticaria a tissue reaction is provokable by the local application of small doses of chemically or biologically specific toxins. Without dogmatizing then, although wheal-like lesions exist in diseases not urticarial, and clearly not due to anaphylaxis, that

disease which is called urticaria may be regarded as being so, among other reasons, because evidence may be adduced of its anaphylactic origin by means of cutaneous tests.

V. SIGNIFICANCE OF THE TESTS

Numerous controls, the combined observations of numerous writers, indicate that positive reactions reveal a peculiarity of the person, otherwise every one would react to all protein, or no one would react to any. It need no longer be reiterated that at least in the majority of cases a percutaneous reaction indicates sensitization, while a negative test does not rule this out. This statement is not to be regarded as dogmatic. Amazing possibilities of confusion exist.

1. *Variations in the Reactions.*—A test may be negative in a sensitized person, perhaps because he has become desensitized, as has been pointed out by Longcope, or after serum sickness. Or it may be positive, as in the case of the orthodox Jew. Mechanical problems also arise. The excoriations may be too superficial, or too deep, introducing fortuitous elements into the wheal. But nevertheless the significance of tests is amenable to some criteria. If a substance indicated by the tests is eliminated from the diet and the patient recovers, as in Case 2 caused by veal and egg yolk, Case 3 caused by buckwheat, Case 6 caused by carrots, the test indicates a great deal. If the suspected substance is ingested, as were carrots in Case 6 and urticaria reappears, the evidence obtained by the tests seems significant. Every one is familiar with instances in which simple foods cause urticaria and on numerous occasions their pathogenicity has been proved by cutaneous tests, notably in buckwheat poisoning and in egg urticaria.

2. *Inconsistencies.*—Inconsistencies depend on mechanical data, as mentioned above, ignorance of foods ingested, as people reacting to substances they deny having eaten, and perhaps, congenital variations making them susceptible or spontaneously sensitized (III, 2, 3 and 8). Perhaps the most important consideration, however, is involved in questions of specificity and group reactions (II, 1 and 2, and III, 10).

VI. PRACTICAL VALUE OF THE TESTS

Other things being equal, and with an understanding of the possible limitations and variations in the test, a positive test, subject to conditions analyzed above, and exceptions to be indicated below, signifies sensitization to a given protein.

1. *Indications of Specificity.*—As Longcope states, and as the work of Schloss and Smith indicates, the tests may be absolutely specific. In serum sickness, however, Longcope found that the test disappeared after the onset of the disease. Unquestionably, a specific test is

obtainable, as Cases 1, 2 and particularly 3, and 6 of our series indicate. In Cases 2, 3 and 6, removal of the indicated articles determined the end of the disease. In Case 4, a large number of foods was implicated, and these foods had been included in diet especially prescribed for the patient's condition. Her first improvement dated from the elimination of the prescribed articles and the substitution of a diet consisting of substances to which she had reacted negatively. The same is true of Case 9, in which tomatoes caused the outbreak. This patient was not observed long enough to have ruled out recurrence.

On the other hand, removing the suspected substances sometimes is without result. In Cases 10 and 12 there was recurrence after improvement. Of the remaining seven cases, Case 1 was not due to food sensitization, but to vegetable substance in cosmetics. The patient recovered when he discontinued the use of these cosmetics. The patients in Cases 7 and 11 were not tested. The remaining four showed features already mentioned, or to be mentioned, but on the whole prejudicial to the value of the tests. Eight of the twelve cases tested, however, support its value.

2. *Limitations of the Test.*—The limitations of the test are perhaps better described as the limitations of our understanding of the test. Nevertheless, we may justifiably conclude that the tests themselves still present some inherent imperfections. In the first place, the proteins used are not those we eat. On the other hand, what we eat is by no means what we absorb, or what sensitizes, but must be some hydrolyzed or cleavage product resulting from digestion. We know, however, that these derivatives inter-react specifically with their parent. We further know, as nearly all our cases reveal, that there is usually sensitization to more than a single substance. The explanation of this has already appeared. In short, it is a matter of group reactions and factors inherent in the concept of split proteins. Moreover, alimentary sensitization depends on anatomic or functional disturbances, and sensitization may continue through introducing chemically like though biologically unlike substances when we attempt to modify diet with regard to suspected foods. In such an eventuality, the disease would necessarily continue. Thus no patient, until more is known of the actual facts, should be given a suspected food, without being observed for attacks of urticaria, and no cure can be expected without adequate treatment of the gastro-intestinal tract, or the latter will continue its rôle as portal of entry.

Some forms of urticaria may not be anaphylactic. This seems unlikely, although possible, as Case 5 shows. A weakly positive response to salmon was elicited in this patient, but ingestion of the suspected substance provoked no attacks. All other food substances gave negative reactions. It is probable that we did not find the right protein in this case.

3. *Value of the Tests.*—The value of the tests may be summed up as follows: Positive reactions indicate sensitization to a protein or certain proteins, as in Cases 2, 3, 4, 6, 9, 10, 11 and 14. In seven of these, the removal from the diet of the single, or the most strikingly reactive of several substances, determined a cure, and in two more, improvement, albeit with recurrence. The significance of negative tests was summed up in the last paragraph of the section preceding this.

4. *Clinical Application of the Tests.*—The limitations of the test are embraced in the newness of the method which requires improvement, in the fact that the urticarial skin is inherently irritable and may give false reactions, and in our ignorance of the clinical significance both of anaphylaxis in man and its demonstrability by local reactions. In addition to this, it requires time and perseverance on the part of both physician and patient, and a great spirit of cooperation on the part of the latter. No more than two dozen tests can be made at a sitting, and thus about seven visits are required, four to complete the series, and two or three more to corroborate the findings. But the method should be pursued, because it promises practical aid in diagnosis and therapy, as our cases show. We do not subscribe at all to Strickler's pessimism, for he worked with too few proteins to justify his condemnation of the procedure. Had it aided us less than it did, we should be loathe to relinquish the method until convinced of its worthlessness. We are convinced of precisely the opposite, and the faintest praise we can accord it is that it at least tends to elide guess work in explaining the cause of urticaria, and in treating the disease.

VII. CONCLUSIONS

1. Are urticaria and allied conditions, notably angioneurotic edema, anaphylactic manifestations? The answer is affirmative, with certain possible exceptions, and sensitization mainly occurs through an anatomically or functionally deranged intestine.

2. Do positive tests prove them to be anaphylactic? This question, too, is answered affirmatively. Sensitization can be demonstrated by local reactions. The qualifications have been discussed.

3. If not, what may their nature be? Possibly, but not probably, they may indicate susceptibility or idiosyncrasy (III, 3 and 4; IV, 3).

4. If not, what do the tests signify? They may indicate merely a tissue reactability required for response to any pathogenic agent, but this is unlikely, for no other diseases except bacterial ones, react in a manner suggesting allergy (IV, 3).

5. What is the practical value of the tests? The practical value of the tests is far reaching. First (V) positive tests indicate sensitization. Second (VI, 1), they show sensitization to certain definite proteins, either singly or in groups.

6. How are they to be clinically applied (VI, 4)? The suspected articles are to be removed from the diet. One by one they should be given to the patient. Those provoking recurrences should be permanently eliminated. Desensitization is to be practiced only as to important foods, and particularly in infants and children in whom the diet is necessarily restricted. No cures can be expected unless the abnormal digestive tract, which is the avenue of sensitization, is treated.

Certain other conclusions that cannot be incorporated in the answers to the six problems must be mentioned.

7. Of sixty-three positive reactions, thirty-seven were to vegetable, twenty-six to animal proteins.

8. Reactions to more than one protein occurred in eleven cases of twelve tested.

9. Reactions to both vegetable and animal proteins occurred in ten cases. In Case 3, however, only buckwheat was tried.

10. Suprarenal extract was of benefit in eight cases, not employed in five, and caused collapse in one.[43]

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[43] In addition to the references already given, the following may be of interest:

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. TOWLE AND HIGHMAN AND MICHAEL

Dr. Hartzell was much pleased by the conversation of the gentlemen who discussed protein sensitization. It was one not only of scientific and academic interest, but of extreme practical importance. Many of the so-called special discoveries and advances in medicine spread from centers like this out to the general practitioner and he did not always use them as they might be used, but abused them. He had recently seen a number of such instances, and within a few weeks had heard a pediatrist state that infantile eczema was nothing but an anaphylactic phenomenon. Dr. Hartzell did not believe this. He had seen for some time past infants and children from 10 to 12 years of age who did not get enough to eat, and their physicians told him they were afraid those children could not digest certain proteins. Dr. Hartzell believed all would agree that urticaria was in the main a phenomenon of anaphylaxis, but was it always so? All had heard of the classic case reported years ago by Hebra in which urticaria could be produced by passing a uterine sound. It was rather difficult to explain this on any theory of anaphylaxis. One of the gentlemen had stated that dermographism was frequently associated with this trouble. Two of the most pronounced examples of dermographism that Dr. Hartzell had seen were associated with pediculosis corporis. In a case seen recently with a most extraordinary dermographism, with the disappearance of the pediculosis the dermographism disappeared promptly.

To return to the question of eczema as an anaphylactic phenomena, one was back to the old question, what is eczema? Dr. Hartzell would not deny that certain types of dermatitis might resemble eczema, but he did not believe that eczema and chronic dermatitis, which we regard as eczema, were of anaphylactic origin.

Dr. Fordyce said one of the most striking examples of the so-called anaphylactic or anaphylactoid reaction to a foreign protein was the case of a man who could not eat shell fish. If he touched the fish with his fork and put the fork in his mouth he would immediately have an outbreak of generalized urticaria. He had repeated this test many times and always with the same result. A young woman developed an outbreak of erythema iris after eating lobster. After three months she ventured again to eat lobster and had an outbreak of bullous erythema involving her face, arms and thighs.

Dr. Fordyce thought attention should be called to the sensitization of the skin that sometimes followed repeated injections of arsphenamin. He had a patient who was treated over three years ago and who developed after his fourth injection of arsphenamin a generalized exfoliative dermatitis. Three years after the dermatitis he was given a small injection of the drug, which was followed within twenty-four hours by an erythematous rash that progressively involved the entire body. His experience had taught him never to repeat the arsphenamin if the patient had previously developed an exfoliative dermatitis following its use. Sensitization to drugs was not alone confined to their internal administration. Analogous conditions have been seen after exposure to liquor formaldehydi. He had recently seen a generalized case of exfoliative dermatitis following the prolonged application of a hair dye which was chemically a paraphenylendiamin compound. This woman suffered for two months from the dermatitis and during part of this time she had an irregular rise of temperature sometimes as high as 103 degrees. She had a leukocytosis of 30,000 and an increase of eosinophils to 30 per cent. Dr. Fordyce desired to emphasize especially the skin allergy after the development of the generalized exfoliative dermatitis from arsenic.

Dr. Smith, apropos of Dr. Fordyce's remarks on sensitization to arsphenamin, recalled the case of a gentleman who was seen by Dr. White and a probable diagnosis of mycosis fungoides made. There were certain syphilitic manifestations and a positive Wassermann reaction; rather small doses of arsphenamin were given. Before this he had received a certain amount of roentgen-ray treatment for his supposed mycosis. Several months after receiving the arsphenamin, he was given Fowler's solution and became sensitized. He then disappeared for approximately two years and returned showing definite late manifestations of syphilis and received 0.3 gm. of arsphenamin. The fact that he had been sensitized to Fowler's solution three years before was overlooked. He promptly developed a severe arsphenamin dermatitis especially over the areas treated before with the roentgen ray. Dr. Smith thought it was surprising that this sensitization had persisted for such a long time.

Dr. Howard Fox spoke of his work in conjunction with Dr. J. Edgar Fisher during the past six months with the protein skin tests. In fifteen cases (other than eczema) of urticaria, erythema multiforme, angioneurotic edema and a few other skin diseases, the practical results had been unsatisfactory. Their experience in sixty cases of adult eczema had also been disappointing. The cutaneous tests with commercial proteins had been used, following the technic of Walker of Boston. Of the sixty cases, nineteen gave positive reactions to one or more proteins. It was rather surprising to find that most of these reactions were given by the proteins of vegetables and cereals.

As most of the patients were private patients it was not feasible, as a rule, to withhold all treatment for several weeks to watch the effect of a modified diet. A striking result occurred in one case in which no treatment was given and merely the reacting foods eliminated from the diet. This patient gave a strong reaction to cabbage and several other foods. After omitting these articles from his diet, his eruption of eight years' duration cleared up for the most part in a short time. It later recurred when, on request, he again ate cabbage. In some cases the results were contradictory. Patients reacted to certain foods, but failed to improve when they were removed from the diet. Dr. Fox said that he and Dr. Fisher finally concluded that the skin tests might ultimately prove of value in a small number of cases of adult eczema.

Dr. Schamberg said that an attempt had been made by certain students of this subject to clarify the atmosphere by assuming two different processes, one an anaphylaxis and the other allergy or hypersensitiveness to nonprotein substances. How much scientific basis there was for this differentiation, it was impossible to say. As Dr. Highman said, certain drugs combine with proteins of the blood and then acquire the properties of proteins; especially was this so with arsphenamin. As soon as it is introduced into the blood it combines with the globulin or protein of the serum. There was a strong parallelism between dermatitis venenata and pollen catarrhs. Many persons suffer with plant poisoning, especially ivy poison, a much greater percentage perhaps than suffer with hay fever. It is impossible to speak with positiveness concerning the nature of the substance that produced the ivy poisons. We know that there is a great variety of antibodies which may be produced in response to the introduction of various antigens into the system. Some are doubtless of the nature of antitoxins. There are two types of cutaneous reactions, one exemplified in the von Pirquet test and the other in the Schick test. A positive von Pirquet reaction means that a specific antibody in the body has reacted with the antigen injected into the skin. With the Schick test it is to determine whether the subject has natural diphtheria antibodies in his body. A positive reaction indicates that there is no antitoxin in the blood to neutralize the injected toxin, whereas a positive reaction with the von Pirquet test means that there are antibodies in the blood. It must be remembered that a positive result in the two tests lead to quite opposite deductions.

As to the practical value of cutaneous food tests, in his experience he had found that in a few instances they have given information of the greatest possible value. In the majority of instances they have proved great disappointments. The type of local reaction varies greatly according to the method employed. If the abrasive method is used the resultant reaction is a wheal, which develops in fifteen minutes, whereas if the intradermal puncture is used the resulting reaction is a nodule, which appears within twenty-four hours.

Dr. Wile said that he would like to inject a little question of doubt into much that had been said in the previous discussion. He thought there had been a loose use of the terms "anaphylaxis" and "sensitization." As he understood anaphylaxis it was not only individual inability to metabolize certain substances, but the term included the ability to transfer similar reactions to laboratory animals passively, by injection of the offending substance and the patient's serum.

Dr. Wile had had the opportunity of discussing with Dr. Schloss, at great length, some years ago the classic case of Dr. Schloss referred to. It was only after the latter was able to produce passive anaphylaxis in laboratory animals, with ovomucoid, the offending substance in egg white, and the patient's serum, that Schloss was satisfied that he had proved out anaphylaxis. The mere percutaneous tests on the skin with various protein substances that might react positively was to his mind not even presumptive evidence that such substances were necessarily anaphylactic to the person. They might suggest occasionally accurately a hypersusceptibility, but, as Dr. Engman had shown, a positive test could occur with certain substances in persons who did not and had never shown idiosyncrasy to such substance.

Dr. Hazen thought it was impossible to study this phenomenon without considering the vegetative nervous system. He remembered a child who had urticaria and this was combined in many instances with bronchial stenosis and asthma. The history, according to the child's mother, was that after riding behind a horse, and after eating eggs and chicken these attacks would come on. Dr. Hazen saw the child in one attack and found that he had a dermatitis, a true bronchial asthma, a true pyloric stenosis, a spastic colon and classic eye changes, and on examination he found that he reacted to the skin tests of horse dandruff, egg albumin and chicken. These had produced an effect on the vagus nerves and the things found clinically were due to vagotonia. At the same time Dr. Hazen did not think one was justified in thinking all these were due to allergy or hypersusceptibility.

A well-known man in Washington had three children, one of whom Dr. Hazen saw a number of years ago because of a dermatitis. Associated with this was pyloric stenosis, bronchial asthma and a spastic colon. A few days before another boy put a dog on him and the father came along and scolded the boy. Within a few minutes the boy had developed all the signs of a vagotonia. In the same family other children developed attacks absolutely similar in every respect, and these attacks could be controlled promptly by the use of atropin. In other words, some of the attacks unquestionably are due to a vagus irritation and this is not always due to a hypersusceptibility or an allergy; in some instances they are due to marked mental irritation. This would explain some of the cases of urticaria when a patient was in a doctor's office, and when a uterine sound was passed. In a case of scabies it was possible that the absorption of the parasite would explain it, due to absorption of the protein, but not necessarily through the food tract.

Dr. Grindon thought it was possible that urticaria might be due to two causes, one anaphylactic and the other nervous in origin. To the latter group probably belonged the case of the girl mentioned by Leloir who developed urticaria whenever she was kissed. While true anaphylaxis differed from sensitization to nonprotein drugs, yet there was a certain relationship between these phenomena. If a person was subject to the one he was probably subject to the other. In a family under his observation for a number of years, a certain lady had urticaria every time she took quinin. A sister was similarly affected. She enjoyed most excellent health except that she was subject to hay fever. On one occasion Dunbar's pollantin, which was a horse serum, was used with considerable relief of the symptoms. Some years later during an attack, a drop was placed in each eye sac and a drop in each nostril. Within a few seconds she became dyspneic, the conjunctivae swelled so that they protruded from the eye clefts and the cornea could be seen at the bottom of a cup. The symptoms were most alarming, but passed off within a few minutes. One of this lady's children was given an immunizing dose of diphtheria antitoxin. Three years later the same child ran a rusty nail into its foot and was given a dose of tetanus antitoxin. Within a short time it was enormously swollen, with the eyes closed tight, the hands and fingers much swollen, and the lips everted. That condition continued off and on for three weeks; it would entirely disappear and then return. After this had been going on for two weeks the child one day suddenly became dyspneic. Epinephrin was at once administered and within a few minutes the respiratory symptoms disappeared, although the skin symptoms continued. This family group showed undoubted sensitization, both to proteins and nonproteins. This might be explained by the protein combination of which Dr. Schamberg has spoken. Another of the children in this family was subject to urticaria from a wide variety of foods.

Dr. Carmichael recalled the case of the infant of a prominent physician in Cincinnati. The child was breast fed for six months without any trouble. At that time the mother became ill and the child was put on bottled milk in small amounts, when it promptly developed urticaria and convulsions and almost died. It was then suggested that goat's milk be substituted for cow's milk. This was procured and the child remained on this diet for eighteen months. It was then brought to Washington and at Dr. Carmichael's suggestion cow's milk was again tried. The child was given one teaspoonful of cow's milk and within a short time a severe urticaria resulted. The child had been tested and now the only positive reactions were for cocoa and grape juice. The child could take cocoa and grape juice.

Dr. Varney thought that desensitization, as the term was being used in the discussion, was the removal of the specific food or sensitizing substance rather than what he understood as desensitization. To desensitize a person would be to render him able to assimilate that article of food without symptoms of sensitization. Infantile eczema probably presents the most definite sensitization picture of any dermatosis. This particular form of dermatitis of infantile eczema is fast being taken from the dermatologist by the pediatrician, largely because of our percentage of failures through, probably, lack of definite methods of determining the specific food or foods that cause the trouble.

Dr. Varney had been interested in attempts at desensitizing infants with chronic eczema of the face by administering small rectal injecions of milk every two or three days. The effect, clinically, within twenty-four hours is first a marked aggravation of the eczema, and then a prompt improvement in about 50 per cent. of the cases.

Dr. Engman said that what he meant by desensitization was the hypodermic injection of extremely small quantities of the offending protein, so that the patient could afterward use that article.

Dr. Hartzell asked whether the gentleman who referred to a dermatitis following arsphenamin thought the dermatitis was evidence of sensitization. Was such a dermatitis never the result of arsenical poisoning?

Dr. Fordyce was of the opinion that the case in which the eruption occurred after three years was due to drug sensitization.

Dr. Stokes had a way of suspecting an external factor in connection with eczema. If the patient started from home with a dermatitis and was nearly well when he arrived at Rochester they studied his environment. An interesting example of this was the case of a man from Tennessee who arrived in pretty bad shape but promptly recovered. He then went home and relapsed. It was found that the dermatitis was due to the ground bone mixture he fed his chickens. He got rid of the dermatitis by getting rid of this brand of chicken food.

Dr. Stokes wished to have Dr. Highman explain the observation of which he thought there were two recorded cases, in which raw egg white caused symptoms, whereas boiled eggs did not. Dr. Stoke's eldest son was an example of this. On the first occasion on receiving a spoonful of egg nog he immediately became cyanotic and greatly swollen, and had alarming symptoms. Since that time he had twice been the victim of raw egg white anaphylaxis. The second time was when some of the nurses went up to his house and decided that the boy had a cowlick which was not becoming and applied egg white in an attempt to improve his appearance. The boy at once developed the most alarming symptoms, a hurry call was sent to his father and when he reached home he found the boy cyanotic, the face tremendously swollen with the lower lip hanging down on the chin and giant wheals over the forehead and in the scalp. This boy could eat hard boiled eggs all the time and have no trouble, but if they were soft boiled he had a prompt response in the form of urticaria.

Dr. Stokes thought the work of Bruno Bloch was interesting in that he reported the transplanting of skin hypersensitive to trichophyton to the varicose ulcer of a patient who was not sensitive. It was found that even after the skin continued to grow on this foreign soil it still retained its sensitiveness to trichophyton.

Dr. Schamberg's mention of a tendency to distinguish between allergy and anaphylaxis reminded him that there was evidence that hypersensitiveness of the skin was not necessarily associated with systemic hypersensitiveness and that accordingly the findings in cutaneous tests could not be interpreted too literally or specifically in regard to the body at large. It was possible to demonstrate that *Spirochaeta pallida* had nothing to do with the positiveness of the luetin test and that the allergy of late syphilis might be imitated in a nonsyphilitic merely by injecting into his skin emulsions of his own skin.

Some recent experimental work by Meyers and his collaborators had tended to show that systemic egg white anaphylaxis in guinea-pigs is not necessarily associated with cutaneous hypersensitiveness to egg white.

Dr. Pusey thought that in this Friday night experience meeting the members had, in their engrossment in giving their own experiences, failed to comment sufficiently on the excellent character of the two papers that opened the discussion, for which he thought the Association was much indebted to the writers. They not only covered the subjects in an exhaustive way, but temperately and wisely. They had, in fact, epitomized all sound information on the subject up to the present. Dr. Pusey gathered that the experiences of most of the gentlemen agreed with his; that specific sensitization tests had not thus far proved of as great practical value as we had hoped they would. He, however, felt that the subject was founded on sound premises and that small as were the practical results at present, there were possibilities of much usefulness in the future.

Dr. Towle (closing) thought the situation could be summed up very well in a phrase—"He damned it with faint praise." He had found great difficulty in writing his paper, in trying to put it in positive terms rather than indefinite terms, and the discussion had corroborated his difficulties.

Dr. Hazen spoke of the vegetative nervous system and tried to draw a sharp line where no sharp line was possible.

Dr. Schamberg spoke of the close relationship between a hypersensitive skin and anaphylaxis. Where does the one begin and the other end? That was the difficulty—they had not stopped to consider what was doing. This was not to deny that anaphylaxis did not exist, but the other also existed and always had. A good example of similar conflict of opinion is found in hysteria. Can it of itself cause actual physical signs? Some authorities say that it can and others that it cannot. A rather illuminating act is that of a Boston man specializing in food testing who has abandoned preparing a special specific substance and has adopted the practice of preparing a single immunizing substance which he gives alike to all patients, and gets equally good results. He labeled it "341" and all the patients got it.

As to the intestinal tract, it is well known that the intestinal tract becomes more permeable in the presence of pathologic conditions. Putrefaction favors congestion, congestion interferes with the normal function of the mucosa, and that favors absorption. The only question that remains to be settled is why patient "A" becomes sensitized to pork and patient "B" refuses to be sensitized. It is evident that there is a foundation somewhere and the profession must find that foundation and then determine what building should be erected on that foundation. The fact should be accepted that physicians know the pros and cons but are utterly ignorant of what goes on between the two.

Dr. Highman (closing) said there was so much to be said that had been inspired by the adequate discussion that it was hard to know where to begin.

As to Dr. Wile's theory, he participated with him in his doubts as to the relationship of anaphylaxis and sensitization in a great many instances, and thought further experimentation was necessary. One experiment by Bruck was significant. He had a patient who was sensitized to pork, so he sensitized a guinea-pig to pork and then injected some of the patient's serum into the guinea-pig and produced anaphylactic shock. That showed how closely in this patient the entire complex held together.

As to the question of Dr. Stokes in regard to the egg white, he thought he could explain that. Anaphylatoxin was destroyed at 100 degrees, which was required to boil an egg hard. He did not know why the eggs would affect some children when they were boiled and some when they were raw, but so far as he was familiar with the literature, hard boiled eggs were not assumed to produce anaphylactic shock.

The question brought up in connection with the relation of hypersusceptibility to anaphylaxis was, Dr. Highman thought, a matter of academic distinction. He believed one should use the term anaphylaxis in a restricted sense as applying solely to protein poisons, and that the types of irritability of the skin seen in response to mercuric chlorid or rhus did represent something in another category. As a matter of fact, even these conditions have the elements of the cutaneous sensitization, because people who were sensitive to ivy or mercuric chlorid or any of the other substances, obviously responded in a manner somewhat similar to what occurred in some forms of food poisoning. The relation of anaphylaxis and the relation of cutaneous sensitization to anaphylaxis were not clearly understood, and, finally, the relation of cutaneous tests to the whole affair was not clearly understood, so we were venturing in a field that as yet had scarcely been explored. For this reason all scientific notions must still necessarily be vague. The whole thing must be considered with a sort of optimistic skepticism. In a series of twelve cases, which he analyzed, eight were illuminated by the test both as to the etiology and therapy. In the next series of twelve this might be reversed. Twelve swallows did not make a summer and twelve cases in a series did not constitute a thesis. We must approach the subject with an open mind. If it proved of value the value would be great, and if it had no value there was certainly no harm in traveling this uncharted sea.

Dr. Engman (closing) said that in egg white sensitization, bread toast could frequently be used, as could hard boiled eggs, when egg white could not be used. He thought words rather than the fundamental principles were being discussed. Was there something in which they could take the offending article which might enter the system and come in contact with the skin? There was, and if not all cases of urticaria were due to it, or all cases of eczema, some undoubtedly were. As men who limit their work to the realm of skin diseases, Dr. Engman felt that dermatologists should thoroughly investigate the subject as others were doing in other branches. The test was very delicate and had to be performed with great care, and it did not always have the same effect on a patient. Findings might be obtained at one time and none the next, and the offending element might not be recognized.

Dr. Markley (closing) said that it was well known that the epidermal products of certain animals may cause general sensitization with the production of asthma or hay fever as well as skin manifestations; under such circumstances the nature of the disorder is usually recognized, but if the skin alone is sensitized it presents a more difficult problem. If the skin is sensitized in local areas the skin test will, of course, be positive in these areas but negative in unsensitized areas, the result being therefore obscure unless multiple tests be made, as pointed out.

LYMPHOGRANULOMATOSIS OF THE SKIN IN HODGKIN'S DISEASE *

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The cutaneous manifestations of Hodgkin's disease may in general be divided into two classes. The first of these includes a group of dermatoses not characteristic of Hodgkin's disease either clinically or histologically. In this class should be mentioned generalized prurigo-like eruptions, pruritus, urticarial, hemorrhagic and bullous eruptions, pigmenation and universal exfoliative erythrodermias. In addition, certain disturbances of nutrition, such as alopecia areata, have been noted. Whether these manifestations are due to the toxic action of the (supposed) infectious agent in Hodgkin's disease, it is not my purpose to discuss. That the prurigo-like eruptions are not characteristic of this disease has been shown by microscopic examinations by Bowen [1] and others. In a woman with typical Hodgkin's disease, Bowen noted prurigo-like lesions on the leg, one of which was examined histologically. He wrote, "It seems to me most rational to regard them as akin to the nodules of true prurigo, as their clinical aspect and histologic structure agree completely with the latter." The second class of cutaneous manifestations of Hodgkin's disease is represented by tumor-like infiltrations with typical histologic structure.

The frequency of the cutaneous manifestations in Hodgkin's disease has been discussed by Cole [2] in a recent paper. He quotes the opinion of Ziegler that "one fourth of all cases of Hodgkin's disease at some time or another in the course of their trouble showed evidence of skin involvement." He also mentions that Westphal found cutaneous lesions in 15 per cent. of his cases. Though at first inclined to think that these figures were rather high, he came to the conclusion, after two years of careful observation of such cases, that they were probably correct.

Manifestations of the skin analogous to those of Hodgkin's disease are seen in the leukemias, particularly of the lymphatic type. Those analogous to the first class (above mentioned prurigo-like

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* From the United States Public Health Service.

* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

[1] Bowen, J. T.: Mycosis Fungoides and Sarcomatosis, J. Cutan. Dis. **15**: 65, 1897.

[2] Cole, H. N.: The Cutaneous Manifestations of Hodgkin's Disease: Lymphogranulomatosis, J. A. M. A. **69**:341 (Aug. 4) 1917.

eruptions, urticaria, etc.) have been spoken of by Audry[3] as leukemids; by Arndt[4] as lymphadenids in contrast to the characteristic infiltration which he calls lymphadenosis.

The case which forms the basis of this communication I hope to show was one of Hodgkin's disease, presenting tumor-like infiltrations of the skin, that is, lesions of the second class mentioned above. The patient was in charge of the U. S. Public Health Service, to whom I am indebted for the privilege of making this report. Every possible help in studying this case has been rendered and the hospital records (Polyclinic Hospital) have been frequently quoted. The patient has been under the immediate care of Dr. Elias A. Reed, chief of the Medical Service, to whom I am especially indebted for assistance.

REPORT OF A CASE

History.—Feb. 5, 1920. The patient, A. H. A., was a man 30 years of age, born in the United States, originally a grocer's clerk. His parents and three sisters were living and healthy. There was no family history of tuberculosis, cancer or any other disease similar to the present one. As a child he had suffered from measles, mumps and diphtheria. He served in the U. S. Marine Corps from 1909 to 1913 and while in Panama, in 1911, contracted malaria. He served as an enlisted man in the United States Army from February, 1914, to March, 1919. He was operated on for hernia in 1917. During the World War he had about ten months' service in France, during which time he suffered from influenza, complicated by pneumonia. He denied venereal disease. His habits were moderate as to alcohol and tobacco. His appetite was good, bowels irregular. He gave no history of rheumatism or attacks of sore throat.

The present illness began in January, 1919, the patient noticing small hard lumps in the neck and scalp. In December, 1919, he was examined by a private physician, who recognized similar lumps in the groin and axillae and recommended the removal of one of them for diagnostic purposes. The result of this examination is given below. A clinical diagnosis of Hodgkin's disease was made at that time. Since May, 1919, the patient had complained of dyspnea on exertion, substernal pressure and a sensation of weight in the abdomen. He has had no dysphagia, night sweats, diarrhea or loss of weight.

Physical Examination.—The patient was a man of medium height, weighing 155 pounds, well nourished and of ruddy complexion. Vision and eyegrounds were normal. The nose showed a deviated septum, enlarged turbinates and hypertrophic rhinitis. The tonsils were slightly enlarged. The ears were normal with the exception of impacted cerumen. Five teeth were missing, four were capped. The lungs were resonant throughout, harsh breathing being heard over the bronchi. The heart was regular as to force and rhythm with no murmurs or thrills. The second pulmonic sound was accentuated. The abdomen was soft, the muscles well developed The spleen could be felt 1 inch below the costal margin, the edge being hard. The liver was felt at the costal border. The kidneys could not be felt. There was considerable tenderness on pressure in the right hypochondriac region. The bones, joints and muscles of the extremities were apparently normal. The reflexes were exaggerated. The blood pressure was systolic 120, diastolic 80. The urine was normal. The Wassermann reaction was negative. Roentgen-ray examination of the chest showed "apices hazy, pulmonary fields clear; mediastinum within normal limits; slight hilus enlargement but no evidence of adenopathy."

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[3] Audry. C.: Sur les leucémides, Ann. de Dermat. et de Syph. **3**:310, 1902.

[4] Arndt, G.: Zur Kenntnis der leukämischen und aleukämischen Lymphadenose (lymphatischen Leukämie und lymphatischen Pseudoleukämie) der Haut mit besonderer Berücksichtigung der klinischen und histologischen Diagnose und Differentialdiagnose, Dermat. Ztschr. **18**:1, 1911.

Examination of the blood on Feb. 12, 1920, showed: hemoglobin, 75 per cent.; red cells, 5,664,000; white cells, 6,600. Differential count: polymorphonuclears, 68; small mononuclears, 27; large mononuclears, 2; eosinophils, 1; basophils, 0; transitionals, 2.

During the two months while the patient was treated at the Polyclinic Hospital (U. S. Public Health Service) he had had a rise of temperature on two occasions (100 and 101 F.) and for a short time his temperature was subnormal.

Examination of Lymphatic Glands.—This showed a moderate enlargement of the lateral and posterior cervical, submaxillary and inguinal groups. They were firm and painless, the overlying skin being normal in appearance and not adherent. The largest gland, about the size of a horse chestnut, was in the posterior cervical region. These were later treated with the roentgen ray and reduced in size. A histologic examination of an excised cervical gland was made in the fall of 1918 by Dr. Warren B. Stone, pathologist of the Ellis Hospital in Schenectady. He reported: "The gland was 0.5 cm. in diameter and exhibited an hyperplasia of lymphoid tissue, together with numerous epithelioid cells and eosinophils. I found also a few giant cells of the Dorothy Reed type and from these findings made a diagnosis of Hodgkin's disease."

Cutaneous Lesions.—These were confined to the face and scalp. They involved practically all of the scalp except the occipital region, half of the right side of the forehead and both temporal regions. They consisted of diffuse, painless, lumpy infiltrations involving the skin and subcutaneous tissue. The surface of the lesions was dry, shiny and of a dull purplish color. There was no evidence of scratching, although the patient complained of occasional slight itching. The most prominent of the tumors was about 2 inches in diameter, elevated about a quarter of an inch above the scalp. On the right side of the forehead was a large, infiltrated, slightly elevated patch, about 3 inches in length, fading from the surrounding normal skin. There were also smaller patches in the temporal regions. There was considerable whitish, branny desquamation scattered over the vertex. There were a few superficial scaly patches on the cheeks. In the midscapular region was a group of a dozen cutaneous nodules of color and consistency similar to those on the scalp. The largest of these was distinctly elevated and about the size of a dime. It was in the region of these nodules that the patient had received about two dozen subcutaneous injections about eight months previously.

HISTOLOGIC EXAMINATION OF THE SKIN

A piece of tissue from the anterior portion of the scalp was excised under local anesthesia on February 17 for histologic examination. This was made by Dr. Walter J. Highman who reported:

Low power (B. & L. eye piece 10, objective 16 mm.); hematoxylin and eosin stain. The epidermis shows no noteworthy abnormalities. There is a diffuse

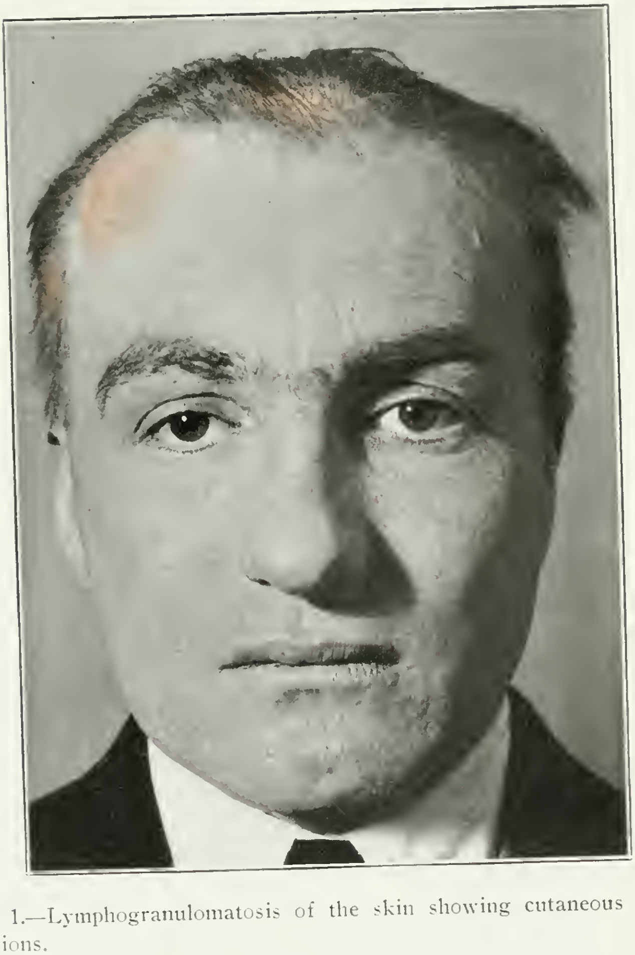

Fig. 1.—Lymphogranulomatosis of the skin showing cutaneous tumor-like infiltrations.

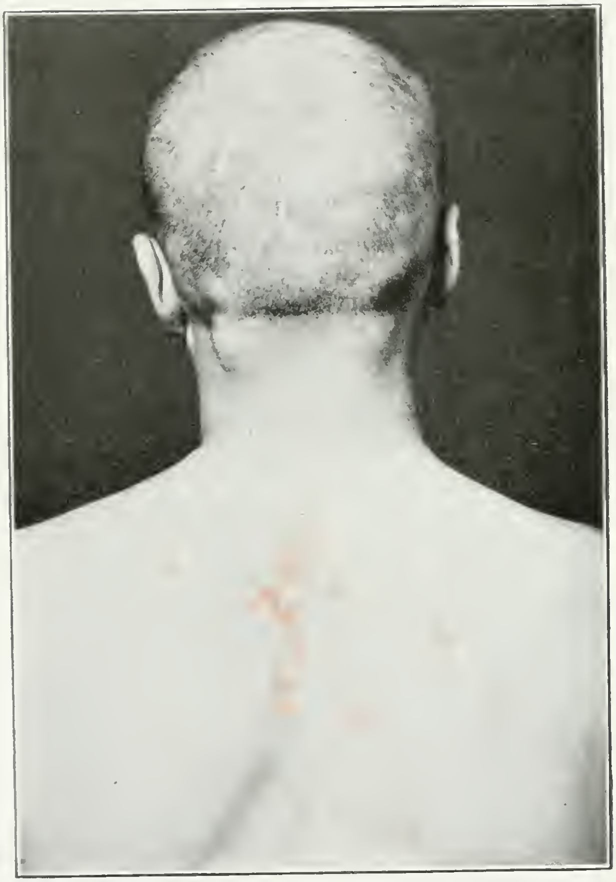

Fig. 2.—Lymphogranulomatosis of the skin and glandular enlargements.

infiltration in the corium from the subpapillary plexus to the utmost depths and although the connective tissue has been disturbed and to a large degree absorbed, the hair content is normal and the arrectores are present.

High power (B. & L. eye piece 10, objective 4 mm.). Under higher magnification the infiltration can roughly be divided into two types, a series of masses, darkly staining uniform cells which are prevailingly perivascular in position, or at least intimately related to the vessels. These groups of cells lie as relatively circumscribed islands in their diffuser, somewhat denser general infiltration. For purposes of convenience let them be called islands and general infiltrations. The island infiltrations consist entirely of cells resembling small lymphocytes as found in the blood, in that they possess a large circular dark nucleus, surrounded by a narrow zone of cytoplasm or apparently none at all. The cells of the general infiltration consist about evenly of the small round type, small and large mononuclear types, with few epithelioid cells and a fairly large number of dividing binucleated cells. There are no plasma cells and no Langhans cells, but mixed with the infiltrations are numerous fibroblasts and an occasional mature connective tissue cell (fixed cells). From time to time, but not in large numbers, an eosinophil cell is observed within the capillaries.

In certain areas there is a great deal of cell detritus, indicating a distinct tendency to necrobiosis. Many uninucleated, large irregular cells not admitting of routine classification are seen. These are probably the mononuclear variety described by Dorothy Reed and Sternberg. Numerous large bodies with three to nine vacuolated, large or small, elongated or rounded nuclei are observed. The size of the cells and their nuclear contents depend on the segment of the cell cut. These suggest Dorothy Reed bodies. The collagen immediately below the epidermis is well preserved throughout the infiltration and is represented by fragments that take the stain relatively faintly. The elastic tissue is preserved in the subpapillary areas; elsewhere it has undergone changes parallel to those of the collagen. The vessels are not increased in number, although the small capillaries throughout are somewhat dilated.

The arterioles are slightly swollen as to all their coats, but show no great thickening as in syphilis. Occasionally the lumen is nearly occluded by edematous endothelial cells. The veins are moderately dilated but otherwise undisturbed. The lymphatics of all types are dilated and engrossed with lymphatic cells already alluded to.

Summary.—The infiltration is lymphogranulomatous and can be only mycosis, or pseudoleukemia (Hodgkin's disease). In mycosis we should expect to find chorioplaques and mitoses in great abundance. In leukemia there would be a greater uniformity of the cells. The presence of Dorothy Reed bodies favors the diagnosis of Hodgkin's disease. If Hodgkin's disease causes skin granuloma containing Dorothy Reed bodies, this must be Hodgkin's disease.

Course and Treatment.—March 8: Roentgen-ray treatment of scalp and forehead was given. Two areas were treated with 1 Holzknecht unit (skin distance) filtered through 3 mm. of aluminum.

March 12: White blood cell count was 7,800; differential count: polymorphonuclears 81, small mononuclears 14, large mononuclears 1, transitionals 1, eosinophils 2, basophils 1.

March 13: Photographs were taken of the head and back.

March 29: Roentgen-ray examination of the chest showed enlarged glands of the left hilus, questionably of the right. No other pathologic condition was observed. The apexes of the lungs appeared normal.

Spinal fluid examination showed 10 cells (mononuclears), the presence of sugar, a faint ring of albumin and a negative Wassermann reaction. Rate of flow was 60 drops per minute. Blood examination revealed: hemoglobin 75 per cent., red cells 4,640,000, white cells 8,600. The differential count was: polymorphonuclears 79, small mononuclears 19, large mononuclears 1, transitionals 0, eosinophils 1, basophils 0. No abnormal cells were present. Blood culture was negative. The blood Wassermann reaction was negative. The Widal reaction was negative and no plasmodia were present.

April 3: Von Pirquet's test was negative.

April 6: Roentgen-ray treatment of the scalp was given. Two areas were rayed with 1 Holzknecht unit (skin distance) filtered through 3 mm. aluminum

April 16: The patient had lost 15 pounds in the past three months.

Histologic examination of the gland: A gland excised from the axilla on March 30 was examined by Dr. Walter J. Highman, who reported that it "showed hyperplasia, the cells being mainly lymphatic. Numerous examples of both forms of the Dorothy Reed bodies were observed, but there were no eosinophils."

OTHER CASES REPORTED

The cases of true Hodgkin's disease of the skin (in the sense of a lymphogranuloma) that have been described in the literature are few in number. Grosz,[5] in 1906, working in Paltauf's laboratory, published his classic paper "On a Hitherto Undescribed Disease of the Skin (Lymphogranulomatosis Cutis)." Since then similar cases have been reported, some of them in great detail, by Hecht,[6] Neumann and Pick,[7] Nobl,[8] Bruusgaard,[9] Ziegler,[10] Arndt,[11] Cole and Trimble.[12]

Alderson's [13] patient, with lesions on the legs resembling gummas, showed the presence microscopically of a lymphogranuloma with numerous eosinophils. Ophuls, who made the histologic examination, said "On account of the numerous eosinophils, the large lymphatic cells and the whole character of the lesions, which resembles the tissue changes in Hodgkin's disease and certain types of lymphosarcoma, the most likely diagnosis to me seems to be Hodgkin's disease—metastatic of leg." The case was not a classic one, however, as there were no "giant cells" and as the lesions underwent necrosis. They did, however, respond favorably to the roentgen ray, a therapeutic agent that is known to have a marked effect on the lymphatic glands and cutaneous tumors of the leukemic group of diseases.

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[5] Grosz, S.: Ueber eine bisher nicht beschriebene Hauterkrankung (Lymphogranulomatosis Cutis), Beitr. z. Path. Anat. (Ziegler) **39**:405, 1906.

[6] Hecht, H.: Ueber lymphogranuloma, Arch. f. Dermat. u. Syph. **98**:107, 1909.

[7] Neumann and Pick: Lymphogranulomatosis Cutis, Deutsch. med. Wchnschr. **35**:2033, 1909.

[8] Nobl, G.: Lymphogranulomatosis Cutis, Wien. klin. Wchnschr. **24**:148, 1911. Ibid.: Lymphogranuloma papulosum disseminatum, Arch. f. Dermat. u. Syph. **110**:487, 1911.

[9] Bruusgaard, E.: Ueber Hauteruptionen bei der myeloiden Leukämie und der malignen Granulomatose, Arch. f. Dermat. u. Syph. **106**:105, 1911.

[10] Ziegler, K.: Die Hodgkinische Krankheit, Jena, 1911.

[11] Arndt, G.: Beitrag zur Kenntnis der Lymphogranulomatose der Haut, Virchows Arch. f. path. Anat. **209**:432, 1912.

[12] Trimble, W. B.: Pseudoleukemia Cutis (Hodgkin's Disease), J. Cutan. Dis. **37**:336, 1919.

[13] Alderson, H. E.: Cutaneous Manifestations in Hodgkin's Disease, J. Cutan Dis. **35**:481, 1917.

Trimble's patient was presented before the Section of Dermatology and Syphilis of the New York Academy of Medicine. As the report of this case in the transactions of the Section was very meager, Dr. Trimble has kindly given me additional information (personal communication) which shows this undoubtedly to be one of lymphogranulomatosis cutis. The patient was a man, 40 years of age, who was suffering from Hodgkin's disease as proved by histologic examination of an excised gland. There were cutaneous lesions on the side of the neck that suggested lupus vulgaris, though on close observation, no apple-jelly nodules were seen. A histologic section of an excised portion of the skin was made and the following condition found by Dr. Alexander Fraser: "In the corium and subcutis are foci composed of lymphocytes, epithelioid cells with a fair number of large multinucleated cells, which are usually regarded as characteristic of Hodgkin's disease. These cells are larger than the epithelioid cells and may have one or several nuclei, which are placed close to each other. The nuclear membrane is distinct and the nuclear chromatin sparse but the nucleoli stain deeply."

In the older literature some cases, as Arndt says, have been described under other titles, which he thinks should be considered in the class of lymphogranulomas. He specifically mentions the case of von Notthaft.[14] Other cases reported under the name of pseudoleukemia, Hodgkin's disease, etc., were not examples of the disease in the sense described later in this paper. These would include the cases of Pfeiffer,[15] Wende,[16] and Arning and Hensel.[17] In the case of Arning and Hensel the characteristic giant cells of lymphogranuloma are neither mentioned in the text nor are they present in the histologic drawings. It may be of interest to add that all, except one of the cases above quoted, occurred in males, following the well known preference of Hodgkin's disease for this sex. In Ziegler's 220 collected cases, more than half were males, while the statistics of Strobel and Hazen[18] showed 80 per cent. of frequency for males.

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[14] Von Notthafft, A.: Ein Fall von Pseudoleukämie, Beitr. z. Path. Anat. (Ziegler) **25**:309, 1899

[15] Pfeiffer, T.: Ein Fall von Pseudoleukämie mit specifischer Erkrankung der Haut, Wien. klin. Wchnschr. **10**:549, 1897.

[16] Wende, G. W.: A Case of Lymphatic Leukemia, Apparently Developing Out of Hodgkin's Disease, Am. J. M. Sc. **122**:836, 1901.

[17] Arning, E., and Hensel, H.: Pseudoleucämia Cutis. Ein Fall von Pseudoleukämie mit Hauttumoren, Ikonographia Dermat., Pt. 4, p. 127, 1909.

CLINICAL DIAGNOSIS IN THE AUTHOR'S CASE

Before discussing the cutaneous lesions of this case, it should first be shown that the patient was suffering from Hodgkin's disease, defining as well as possible the current conception of this affection. That there has been a great deal of confusion regarding the nature of Hodgkin's disease, first described in 1832, is evident from the many names that have been used to describe it. These include Hodgkin's disease (Wilks); progressive multiple lymph gland hypertrophy (Wunderlich); pseudoleukemia (Cohnheim); lymphosarcoma (Virchow); malignant lymphosarcoma (Langhans); desmoid carcinoma (Schultz); lymphogranulomatosis (Sternberg-Paltauf); lymphomatosis granulomatose (E. Fraenkel); malignant granuloma (Benda). The disease is defined by Longcope[19] as "an affection characterized by painless progressive enlargement, usually of several groups of lymph nodes and accompanied by a progressive anemia. Often the spleen and sometimes the liver are enlarged." In regard to the blood findings he says that there is "no constant or characteristic alteration." Other symptoms such as intermittent, remittent or at times continued fever, cachexia, night sweats, etc., briefly make up the clinical picture. Lymphatic leukemia is practically ruled out in my case by the negative blood findings, although it must be admitted that a lymphatic leukemia may for a time be aleukemic. Though Gulland and Goodall[20] scoff at the idea of an aleukemic leukemia, it is accepted by the majority of authorities. Naegeli[21] says the detection of a leukemia in this stage can generally, but unfortunately not always, be made from the presence of a marked relative lymphocytosis and the presence of pathologic types of leukocytes. The diagnostic value of these abnormal cells is also mentioned by Grawitz,[22] Ward,[23] and others.

Clinically my patient showed a painless, rather slight enlargement of most of the palpable lymphatic glands, a well-marked enlargement of the spleen, a mild anemia but otherwise normal blood picture, occasional fever, dyspnea and some asthenia. The clinical diagnosis of Hodgkin's disease was therefore highly probable. This was established by the microscopic examination of an excised gland.

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[18] Strobel, E. R., and Hazen, H. H.: Mycosis Fungoides in the Negro, J. Cutan. Dis. **29**:147, 1911.

[19] Longcope, W. T.: Hodgkin's Disease, Modern Medicine (Osler and McCrae), Philadelphia, Lea & Febiger, 1915.

[20] Gulland, G. L., and Goodall, A.: The Blood: A Guide to Its Examination and to the Diagnosis and Treatment of Its Diseases, E. B. Treat, 1912.

[21] Naegeli, O.: Blutkrankheiten und Blutdiagnostik, Leipzig, 1912.

[22] Grawitz, E.: Klinische Pathologie des Blutes, Berlin, 1902.

[23] Ward, G. R.: Clinical Haematology, Philadelphia, W. B. Saunders Company, 1914.

PATHOLOGIC CONCEPTION OF HODGKIN'S DISEASE

It is necessary at this point to refer to the histologic findings, which at the present time are considered by many as characteristic of Hodgkin's disease. According to MacCallum[24] "the new tissue produced has a constant histologic character which is easy to distinguish from that seen in any other condition." Longcope[25] states that the first marked change in the smallest glands is an hyperplasia of the lymphoid cells. The reticular tissue becomes coarser and increased in amount and later almost all of its normal structure is lost. The reticulum then forms a coarse network enclosing cells of different types, narrow bands and young connective tissue dividing the glands into irregular lobules. In the reticular network are found large and small lymphocytes, plasma cells, polymorphonuclear and eosinophil leukocytes, epithelioid cells and finally the characteristic uninuclear and mononuclear giant cells. The connective tissue increases as the disease progresses. While the structures are very cellular at first, they ultimately change almost to fibrous tissue.

The peculiar giant cells mentioned were minutely described by Dorothy Reed[26] in 1902 and are often spoken of in this country as Dorothy Reed cells. Similar cells had been previously described by Sternberg,[27] and among German writers they have since borne his name. In speaking of Sternberg's article written in 1898, Reed says: "The histologic peculiarities of the growth from his descriptions and infiltrations agree closely with the changes met with in our series." Reed's description of the peculiar giant cells is in part as follows:

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[24] MacCallum, W. G.: On the Pathological Anatomy of Lymphosarcoma and Its Status with Relation to Hodgkin's Disease, Bull. John Hopkins Hosp. **18**:337, 1907.

[25] Longcope, W. T.: On the Pathological Histology of Hodgkin's Disease, with a Report of a Series of Cases, Bull. of Ayer Clin. Lab. of Penn. Hosp. **1**:4, 1903.

[26] Reed, D. M.: On the Pathological Changes in Hodgkin's Disease, with Especial Reference to Its Relation to Tuberculosis, Johns Hopkins Hosp. Reports **10**:133, 1902.

[27] Sternberg, C.: Ueber eine eigenartige unter dem Bilde der Pseudoleukämie, verlaufende Tuberkulose des lymphatischen Apparates, Ztschr. f. Heilk. **19**:21, 1898.

> They vary from the size of two or three red blood corpuscles to cells twenty times this size. They usually lie free in the interstices of the tissues but we occasionally see them in the reticulum and with irregular protoplasmic processes. The nucleus is usually large in proportion to the size of the cell. It may be single or multiple. If single, it is usually round. Bean shaped and irregularly indented nuclei are common. If multiple, the nuclei may be arranged peripherally in the cell or heaped in the center. Eight or ten have been seen in a single cell. The chromatin network is prominent in these nuclei and one or more large nuclei are always present. The nucleoli always take a contrasting stain to the nucleus. No definite mitotic forms were ever seen. Direct division was frequently observed. The protoplasm is usually homogeneous and stains well. These giant cells, so far as our observation reaches, are peculiar to this growth and are of great assistance in diagnosis.

The work of Reed on the histologic findings in Hodgkin's disease, including the characteristic giant cells, was soon corroborated by Longcope, Simmons,[28] Gibbons,[29] MacCallum, etc. Later Symmers[30] wrote: "In late years Hodgkin's disease appears to have been recognized as a definite histologic entity, characterized by changes which resemble those of the infective granulomas." He suggested as a name for the disease "Hodgkin's granulomatous lymphoma."

Warthin[31] considers that the pathologic conception above described is not typical of all cases of Hodgkin's disease. He has found these changes in only one third of the cases in which the clinical diagnosis of Hodgkin's disease was made. He states that the various forms of generalized and regional lymphocytoma are regarded by some as Hodgkin's disease or pseudoleukemia. Other writers (Reed, Longcope, MacCallum) he says regard as the essential histologic changes a very different process. This is characterized by changes resembling a chronic inflammatory process, consisting of proliferation of endothelial and reticular cells, the presence of many eosinophils and a progressive fibrosis. He agrees that such a pathologic condition exists. He thinks "at the present moment it would appear wisest to limit the pathologic diagnosis of Hodgkin's disease to the chronic inflammatory type of Reed, Longcope, and others, until its etiologic nature is discovered." It is convenient to speak of it, he says, as the endothelioid type of Hodgkin's disease. If this perhaps limited, but definite conception, is accepted as typical of Hodgkin's disease, there seems no doubt that my case is pathologically one of this class. That it was probably a case of Hodgkin's disease, as shown by the clinical findings, has already been stated.

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[28] Simmons, C. C.: Hodgkin's Disease. A Pathological Analysis of Nine Cases, J. M. Res. 1903, 4 New Series, p. 378.

[29] Gibbons, H. W.: The Relation of Hodgkin's Disease to Lymphosarcoma, Am. J. M. Sc. **132**:692, 1906.

[30] Symmers, Douglas: Certain Unusual Lesions of the Lymphatic Apparatus, Arch. Int. Med. **4**:218 (Sept.) 1909.

[31] Warthin, A. S.: Osler's Modern Medicine, Philadelphia, Lea & Febiger, **4**:729, 1908.

DISCUSSION OF THE AUTHOR'S CASE

In discussing the cutaneous lesions presented in my case, it is necessary to consider the possibility of lymphatic leukemia and mycosis fungoides. A lymphatic leukemia can be almost surely ruled out by the blood picture, as there was no actual or relative increase in the number of lymphocytes. It can surely be ruled out from the histologic findings of a lymphogranuloma. In regard to mycosis fungoides the

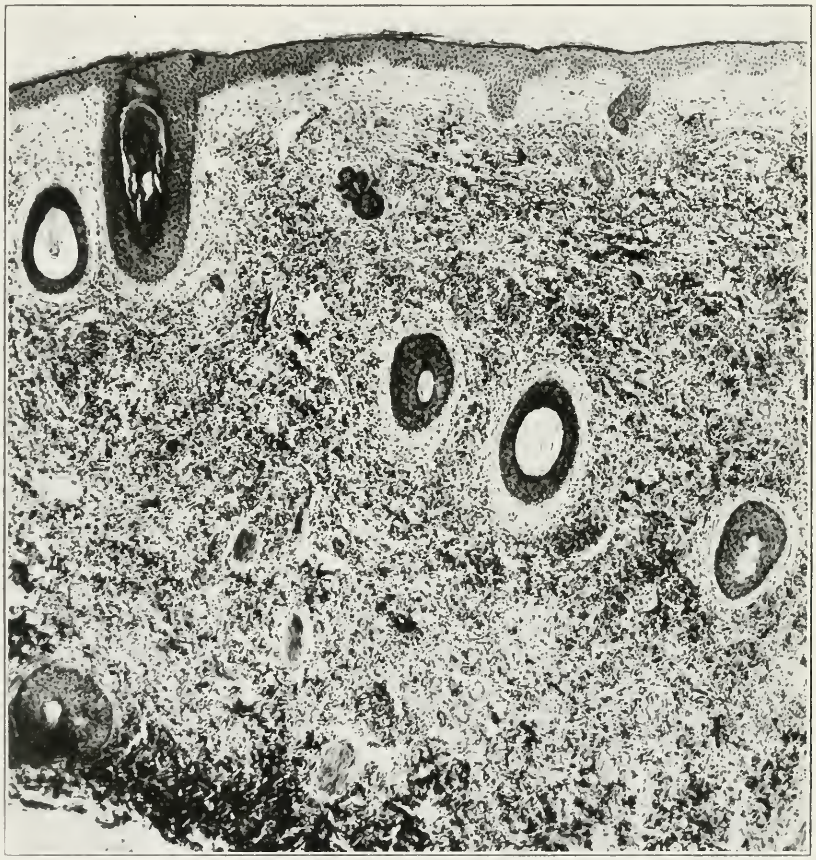

Fig. 3.—Low power. The infiltration extends from the subpapillary vascular plexus to the utmost depths of the tissue and consists of large masses of lymphocytes situated mostly about the vessels. There is a dense background of general infiltration of the same character; the vessels and adnexa are virtually unchanged.

problem is more difficult. However, the mode of onset (appearance of tumors without preceding eczematoid or other lesions), the involvement of the lymphatic glands and spleen and the virtual absence of itching, all are against the clinical diagnosis of mycosis fungoides. The presence of the characteristic giant cells in the skin, together with the histologic findings in the lymphatic glands, are strong evidence of a true case of Hodgkin's disease of the skin in the pathologic sense already described.

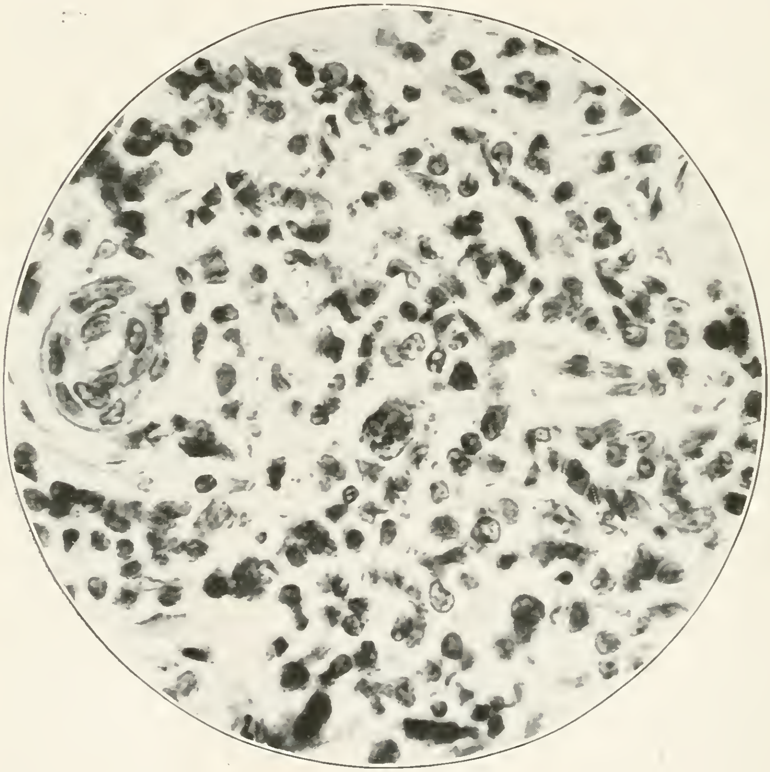

Fig. 4.—High power. In the center of the field is a Dorothy Reed cell. The lymphocytes, particularly in relation to the vessel, are clearly shown.

The patient was presented on February 24 before the New York Dermatological Society (before the result of the biopsy was known) and on March 22 before the dermatological section of the New York Academy of Medicine. At the latter meeting, after describing the histologic findings recorded in this report, Dr. Walter J. Highman said in conclusion that "these findings convince me that the case is one of Hodgkin's disease."

Dr. J. F. Fraser, in discussing the case, said in part that lesions presenting the typical histologic picture of Hodgkin's disease were of very rare occurrence in the skin. He had observed only one case in which the typical Hodgkin's lesion was present in the true skin (Trimble's case quoted above). He believed that many of the cases that had been reported as nodules in the skin were not lesions of the true skin at all but nodes of the subcutis. One of his cases had illustrated this point very well. He said that since Dr. Highman had explained the findings of the characteristic picture in the skin lesions, he was willing to accept a diagnosis of Hodgkin's disease; the so-called Dorothy Reed cell, so far as he was aware, was not found in any other condition. He added that the case "should be recorded in the literature as one showing the typical Hodgkin's disease lesions in the skin."

RELATIONSHIP OF HODGKIN'S DISEASE TO MYCOSIS FUNGOIDES

It may be of interest to touch on the difficult and much discussed subject of the relationship of mycosis fungoides to Hodgkin's disease. Some writers have considered mycosis fungoides a cutaneous form of Hodgkin's disease, an opinion expressed by Ziegler in his monograph. Strobel and Hazen think that mycosis fungoides belongs to the group of lymphomas, including Hodgkin's disease. They state that the "type of Hodgkin's disease, as described by Reed, Longcope and others is essentially different from mycosis fungoides, especially if one regards the epithelioid and giant cells as being really essential characteristics of true Hodgkin's disease." They think, however, that "the essential pathologic picture is the lymphoid proliferation and that the other cell types constitute merely an unimportant variation."

It would appear that mycosis fungoides and Hodgkin's disease are separate clinical, if not pathologic, entities. In the excellent comparative tables of Strobel and Hazen the similarities of the two affections in many respects are rather striking. Mycosis fungoides, however, appears primarily as a disease of the skin, whereas Hodgkin's disease primarily affects the lymphatic glands. The tumors of mycosis, except in rare cases of so-called mycosis fungoides d'emblée (Vidal and Brocq[32]), are preceded by eczematoid and sharply defined erythematous (frequently circinate) lesions. These prefungoid eruptions are not merely incidental, as they show the histologic picture of the disease; they are in fact an early stage of the disease of which the tumors are a later development. The cutaneous manifestations of Hodgkin's disease other than the tumor-like infiltration are the incidental, nonspecific eruptions, most often of a prurigo-like or urticarial type. In mycosis fungoides there is always a tendency to necrosis and ulceration, which is not seen in Hodgkin's disease. Another important distinction is the involvement of the spleen, liver and other internal organs (mediastinum as shown by the roentgen ray) which, except in rare instances, has not been noted in mycosis fungoides. Pruritus of great severity is a classic symptom of the prefungoid eruption but this may also accompany the cutaneous lesions of Hodgkin's disease, and indeed occurs in this affection without any visible lesions of the skin.

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[32] Vidal, E., and Brocq, L.: Etude sur le mycosis fongoide, La France méd. **2**:946, 1885.

The opinion expressed by Ziegler that mycosis fungoides represents a cutaneous form of Hodgkin's disease was arrived at from certain resemblances in the histologic picture. Actuated by Ziegler's statement, Arndt reexamined in a critical manner the histologic material from nine cases of mycosis in different periods of development. In all of his cases, some of them studied for several years, a clinical diagnosis of mycosis fungoides had been made. In the "eczematoid" and "flat infiltration" stages he found giant cells corresponding to those of the Sternberg type, except that they were much fewer in number than in Hodgkin's disease. In the nodules and tumors of mycosis, on the other hand, they were entirely absent or only occasionally found after most painstaking search. He also stated that eosinophils are at times present in the early stages of both diseases, but only exceptionally in the tumor stage of mycosis. As they were at times so numerous in the lymph nodes and inner organs, Pick suggested as a new name for Hodgkin's disease "granuloma gigantocellulare eosinophilicum." This condition, it may be added, was not present in my case. Whether the peculiar giant cells of Sternberg (corresponding to the cells described by Reed) are absolutely specific for Hodgkin's disease, Arndt said was not settled, and mentioned Schridde as authority for saying that morphologically identical cells were occasionally present in other granulation tissue. Arndt thought that the characteristic picture of Hodgkin's disease was shown by a profusion of giant cells, polymorphism of the cellular infiltrate and the eosinophilia. In the majority of cases that had been histologically proved as Hodgkin's disease, Arndt continued, the clinical picture of classic mycosis had not been present. On the other hand, such cases had always shown glandular changes, frequently changes in the liver and spleen, fever cachexia, etc., which, entirely apart from the skin lesions, made the diagnosis of Hodgkin's disease probable.

The difficulties that are at times encountered in differentiating both clinically and pathologically between mycosis fungoides and Hodgkin's disease are well illustrated in a recent article by Dr. J. F. Fraser[33] on the pathology of mycosis fungoides. In one of his seven cases a definite picture of early mycosis was shown by the mode of onset and development, though the case finally showed "clinical and pathologic features indicative of Hodgkin's disease." In analyzing the case, he concluded that the "facts exclude the interpretation of the case as one of Hodgkin's disease with premycosic skin manifestations." He was left with the following three alternatives: (1) that the two diseases existed independently in his case; (2) that they are different manifestations of the same disease; (3) or that they are different diseases caused by agents that can, under certain conditions, stimulate the tissues to very similar reactions. Though unable to decide on one of these hypotheses, he appeared to incline somewhat to the last interpretation.

From the preceding it seems clear that the histologic differentiation between mycosis fungoides and Hodgkin's disease may be very difficult. Whether mycosis should be considered as a cutaneous manifestation of Hodgkin's disease cannot be settled positively until the cause of these diseases has been discovered. That Hodgkin's disease has a "very precise histology" but a "wholly unknown etiology" is the opinion of Janeway.[34] In spite of Bunting and Yates' work, the etiology he says "cannot be considered solved for Hodgkin's disease."

RELATIONSHIP OF HODGKIN'S DISEASE TO TUBERCULOSIS

Finally, regarding the relationship of Hodgkin's disease to tuberculosis: In my case there were no findings that suggested that the disease process was in any way related to tuberculosis. The publication of Sternberg's paper in 1898 was the source of much discussion concerning this relationship, though Fischer[35] had previously concluded on clinical grounds that the Sternberg disease had no relationship to tuberculosis. Space will not permit further mention of this question, which has been thoroughly discussed by Ziegler, Myer[36] and others. In my own case there was no family history of tuberculosis. There was no history of cough, bloody expectoration, night sweats, etc., and a physical examination of the chest was negative. Though the first examination of the lungs showed "apices hazy," subsequent roentgenograms of the lungs failed to show, on careful scrutiny, anything abnormal. The von Pirquet reaction was negative and examination of the spinal fluid showed nothing abnormal. The histologic structure of both glands and cutaneous tumors failed to show either the presence of tubercle bacilli or any structure such as Langhans' giant cells, caseation, etc., suggesting tuberculosis. The result of guinea-pig inoculation of tissue from an excised gland could not be given at the time of reading this paper as the intervening period (four weeks) was not sufficiently long. Guinea-pig killed June 1. Necropsy showed no signs of tuberculosis.

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[33] 33. Fraser, J. F.: The Pathology of Mycosis Fungoides, J. Cutan. Dis. **35**:793, 1917.

[34] 34. Janeway, T. C.: Hodgkin's Disease with Extensive Skin Eruption, Med. Clin. North America **1**:1, 1917.

[35] 35. Fischer, F.: Ueber malignes Lymphom, Arch. f. klin. Chir. **55**:467, 1897.

[36] 36. Myer, O.: Beitrage zur Klinik, Pathogenese und pathologischen Anatome des malignen Granuloms, Frankfort. Ztschr. f. Pathol. **8**:343, 1911.

SUMMARY OF CASE

The patient whose history forms the basis of this report was an ex-soldier of the regular Army, 30 years of age, who presented a moderate, painless enlargement of various groups of lymphatic glands, enlargement of the spleen and liver, a normal blood picture, except for a mild anemia, dyspnea on exertion and increasing asthenia. At the time of writing, his illness had existed fifteen months. A histologic examination of an excised gland showed a typical picture of a lymphogranuloma, including the presence of uninuclear and multinuclear giant cells of the Dorothy Reed type. The cutaneous lesions consisted of tumor-like infiltrations of portions of the scalp, forehead and midscapular region. Histologic examination of a tumor from the scalp showed a similar structure to that of the gland. No increase of eosinophils was present in either gland or cutaneous tumor. Thorough examination (physical, roentgen-ray and pathologic) failed to show any evidence of tuberculosis.

CONCLUSIONS

1. If the pathologic conception of Hodgkin's disease is limited to what Warthin speaks of as the "endothelial type," meaning the conditions described by Reed, Longcope and others, this case must be regarded as one of Hodgkin's disease.

2. As the cutaneous lesions showed a similar structure to that found in lymphatic glands, it should be classed as one of true Hodgkin's disease of the skin. This condition has been previously reported in only a small number of cases.

3. This case may be added to those that tend to disprove the contention that Hodgkin's disease is related to tuberculosis.

4. Mycosis fungoides can generally be clinically differentiated from Hodgkin's disease, though at times this may be difficult or impossible. The differential diagnosis, from the histologic standpoint, may also be difficult at a given moment. Until the causes of these diseases are definitely ascertained, it cannot be settled with certainty whether mycosis fungoides should be considered as a cutaneous manifestation of Hodgkin's disease.

In addition to the acknowledgment I have made in this report to those who have given me assistance, I wish to express my thanks to Dr. George M. MacKee for making the photomicrographs and to Drs. W. T. Longcope and S. Pollitzer for reading my manuscript and making valuable suggestions.

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LYMPHATIC LEUKEMIA WITH PRIMARY MANIFESTATIONS OF THE SKIN *

JOHN BUTLER, M.D.

MINNEAPOLIS

In lymphatic leukemia occasionally there are found lymphadenotic infiltrations in the skin and subcutaneous tissues that are a part of the general disease. These infiltrations consist of hyperplastic lymphocytic elements and are generally supposed to be marrow lymphocytes transported by the blood stream and deposited in the skin and subcutaneous tissues. These lymphadenotic skin changes occurring in, or preceding, a lymphatic leukemia are of two forms: the circumscribed, or tumor, and the diffuse, or universal. The first is a nodular, or tumor form, or a circumscribed leukemic, or aleukemic, lymphadenosis of the skin. The second is a diffuse or universal leukemic, or aleukemic, lymphadenosis of the skin. Sometimes we find generalized skin affections, as purpura, prurigo, urticaria, pruritus and generalized exfoliative dermatitis, associated with or preceding a leukemic condition. The differentiation of this group of affections from like processes in no way related to a leukemia is impossible by means of clinical and histologic studies only, and every patient showing such chronic lesions, in the absence of an etiologic factor, should have a blood examination at different times to determine the possible existence of a leukemia. In a recent paper by Arndt,[1] he discusses skin changes in leukemic conditions; he suggested a revision of the nomenclature by dropping the terms lymphatic, and myelogenous, leukemia for the reason that the blood in cases so designated may be normal at times. He recommended as a substitute the terms leukemic, aleukemic and subleukemic lymphadenosis, which would allow a correct comparison of the blood changes with the lymphadenotic changes in the various organs involved. Therefore he designates according to the blood picture: First, aleukemic lymphadenosis when the organs are infiltrated and the blood picture is normal; second, subleukemic lymphadenosis, if the number of white cells in the blood is normal or very little increased but the proportion of the lymphocytes is increased; and third, leukemic lymphadenosis when there is an absolute permanent progressive increase of lymphocytes in the blood and the total number of leukocytes is augmented.

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

[1] Arndt, G.: Dermat. Ztschr. **18**:53, 1911; Diseases and New Growths of Lymphatic Origin, J. A. M. A. **63**:1268 (Oct. 10) 1914.

Strobel, E. R., and Hazen, H. H.: J. Cutan. Dis. **29**:147, 1911.

These lymphadenotic skin changes are in no way synchronous with or dependent on the blood changes and they may be the first and only recognizable symptom of leukemia or preleukemia. Therefore, in considering skin affections that may be of leukemic nature, it is important to bear in mind that the blood picture may be absolutely indifferent to the aspect or cytology of the cutaneous lesions. The evolution of the skin lesions generally follows the evolution of the leukemia; however, they may occur at any time, sometimes in the beginning, sometimes in the course of the disease or in the final stage. They may occur before or after lymphatic, glandular or splenic involvement. They precede the blood changes in many cases, which may lead us to consider the cutaneous foci the starting point of the disease. If there is visceral hypertrophy, it may escape notice and the cutaneous affection not only may be the first symptom to appear, but may seem independent of visceral change, and the visceral involvement may only be evident at necropsy. Sometimes the cutaneous manifestations in leukemia are neglected by both patient and physician and are considered as trivial incidents, or they may dominate and mask the general malady. This surely emphasizes the importance of a careful examination in diseases characterized by skin affections which may be associated with alterations in the hematopoietic system.

A histologic examination of the lesions in the circumscribed form reveals alterations that consist of a dense and compact infiltrate which has the morphologic qualities of small or large lymphocytes; accumulations of these lymphocytes occur around the vessels, principally where the blood supply is abundant, as around the follicles and glands. These lymphatic foci coalesce and form infiltrative masses. There is a very sparse production of connective tissue in the vicinity of such lymphadenotic formations. The process spreads about the vessels to the reticular dermis and the subcutaneous tissues; there is a zone of normal texture between the reticular layer and the epidermis.

The histology of the diffuse or universal lymphadenosis of the skin discloses similar alterations, but it differs in this, that there are diffusions in the whole cutaneous integument; the original connective tissue is pushed aside and replaced by lymphocytes and there is no proliferation of the connective tissue. We find a pronounced cellular polymorphia, numerous small lymphatic lymphoblasts and more rarely large and atypic forms; the papillary and subpapillary layers show dilated blood vessels and pronounced edema with little or no infiltrations. Numerous mitoses may be observed in these cases in contradistinction to the circumscribed type, where they are rarely observed.

Up to the present time there have been recorded in all of the available literature less than one hundred cases of lymphatic leukemia with associated lymphadenotic skin lesions. Of those recorded, about half were observed in cases of acute lymphatic leukemia and about the same number in the chronic type. In most of these cases, the blood changes preceded the skin changes. About 90 per cent. of all the contributions on leukemic skin affections are reported in the German, French and Italian literature.

I report herewith a case of lymphatic leukemia following lymphadenotic skin changes of the circumscribed or tumor type. There were many interesting features in connection with this case that may be summarized before describing it in detail. The disease began apparently with a throat infection. The first evidence of the disease was the development of the skin tumors. The blood picture was normal at the beginning of the disease. There were no blood changes until all of the skin tumors were formed. Glandular and visceral involvement was not apparent in this case at any time. The skin tumors were made up of collections of large lymphocytes. When all the tumors were formed the blood showed a leukemia for the first time. The lymphocytic deposits showed numerous mitoses. The benzol treatment caused a partial regression and paling of the tumors.

REPORT OF CASE

History.—Miss R., aged 35 years, was first seen by Dr. W. J. Byrnes, April 14, 1916. Her father died of pneumonia at the age of 56. She was survived by her mother, three sisters and two brothers, all of whom were in the best of health. The patient had always been in excellent health except for an attack of diphtheria at 12 years; since that time she had not known a sick day until April 14, when she called on Dr. Byrnes. She complained at that time of a slight sore throat and some pain in the back of the neck and in the right shoulder. She had a temperature of 101 F., and the condition was assumed to be rheumatic. The pain in the neck and shoulder diminished in a few days and the temperature became normal. On April 29, she had another attack of sore throat and a temperature ranging between 102 and 104 F., which lasted for three days. While Dr. Byrnes was attending her for this attack she called his attention to a painless subcutaneous tumor, the size of a dime, on the flexor surface of the right forearm. This tumor involved the overlying skin, was slightly raised and reddish brown. Dr. Byrnes made a careful examination and could discern no other tumors, cutaneous or subcutaneous. The sudden rise of temperature of three days' duration dropped to normal, and the patient felt comfortable. A few days later, there developed two similar tumors under the right shoulder blade and three over the sternum. At this time, she showed a slight loss of weight, she became slightly pale and the temperature was normal in the morning but ranged between 99 and 100 in the afternoon. The last week in May, approximately one month after first calling on her physician, numerous tumors began to develop on the face and extremities. These tumors were more readily palpated than seen and the overlying skin was of normal color. A blood examination was made at this time, but revealed no abnormalities.

Examination.—From this time on the tumors began to take on a livid red color, and the patient began to show marked anemia and weakness. The tumors multiplied rapidly, and the patient was confined to her bed. I saw her in

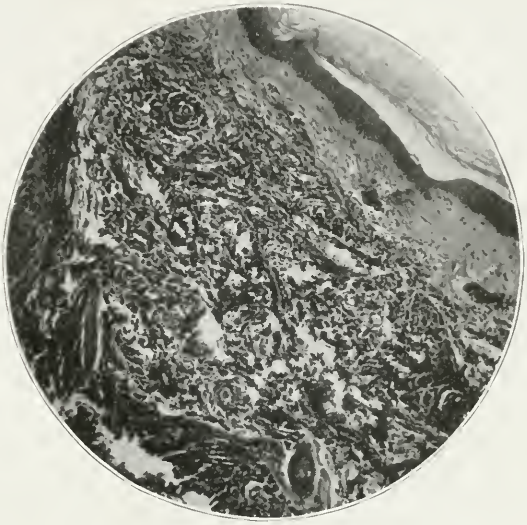

Fig. 1.—Section of nodule under low magnification, showing the small cords and nests of lymphocytes in the superficial part, separated by a fibrous connective tissue. The cell nests in the deeper portion are larger.

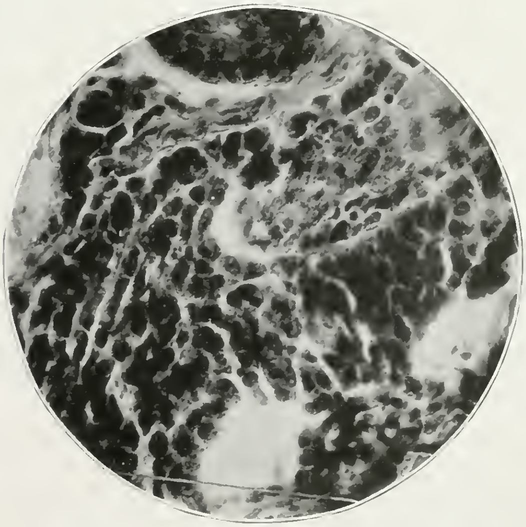

Fig. 2.—Large cell nest from deeper part of nodule under high magnification. The cells are of lymphatic type and are closely packed.

consultation with Dr. Byrnes on July 19, 1916. She was a slender woman weighing about 115 pounds; her normal weight was 130 pounds. The first impression on looking at her was the striking resemblance of her face to the characteristic leonine facies of the leper; the extreme paleness was the only distinguishing feature that would make one hesitate in making a snap diagnosis of nodular leprosy. Closer examination revealed the presence of from twenty-five to thirty subcutaneous tumors, varying in size from that of a pea to that of a hazelnut, which were of a waxy, gray-yellow translucent appearance and doughy in consistency. The tumors protruded slightly above the skin surface. Many of them involved the skin, others were subcutaneous, not visible, but easily palpable. They were most numerous on the eyebrows, eyelids and forehead, where they raised the skin in folds. The cheeks were singularly free; the chin and neck showed more circumscribed formations. The lymphatic ring around the mouth was evenly infiltrated, suggesting a ring of coalesced subcutaneous tumors. The body presented about 500 such tumors. These were much larger than the lesions on the face, measuring from 2 to 5 cm. in diameter. They were rather flat-topped, round or oval raised patches of firmer consistency than the tumors on the face. The skin between the tumors appeared normal. All of the tumors on the body were a cyanotic or livid red. On the extremities, the tumors were somewhat smaller and oval in contour, and of even firmer consistency than the body lesions. Their color varied from a rose red to a cyanotic reddish-brown or blue. The lesions around the feet were larger and their borders were of a grayish blue with a hemorrhagic border, not unlike the patchy lesions observed in Kaposi's hemorrhagic sarcoma. A notable peculiarity of the tumors on the body and extremity was that the benzol treatment would make the color fade from them temporarily, so that they resembled the face lesions in color at times.

RESULTS OF BLOOD EXAMINATION

	Disp. Clinic July 15	Dr. Head July 28	Dr. White Sept. 1	Dr. Head Sept. 5	Dr. Rizer Sept. 12
Hemoglobin	65%	55%		24%	25%
Erythrocytes	3,200,000	2,750 000	1,496,000	1,900,000	1,500,000
Leukocytes	5,000	3,000	40,730	52,000	52,800
Polymorphonuclears	63%	67%	2.6%	3.5%	3.5%
Large lymphocytes	2%	3.5%	77%	91.5%	92%
Small lymphocytes	29%	26%	12%	4.5%	4.5%
Transitionals	1	0.5		0.5	
Eosinophils	4.0	2%		0.0	
Myelocytes		0.0			0.0
Normoblasts	....	....	....	1 in 200 cells	
Megaloblasts	....	2 in 200 cells	....	1 in 200 cells	
Poikilocytosis	....	present	....	0.0	moderate
Anisocytosis	....	present	....	present	moderate
Extruded nuclei	....	....	8.3	....	No nucleated reds

Dr. George Douglas Head saw this patient with me on July 20, when he made a complete physical examination. He kindly gave me his findings, which are as follows:

The patient, an intelligent girl, was tall and thin. The pupils reacted to light, the knee jerks were present.[2] There was no swelling to be made out along the long bones. A careful examination was made for enlarged lymph glands or metastatic growths in the bones, but none could be found. The spleen was just palpable at the costal margin; the liver was not enlarged. No distinct masses could be made out in the abdomen. The patient's tongue was fairly clean. There was no swelling of the lower limbs. The patient was distinctly emaciated. The heart was negative; nothing was made out in the lungs; there was no cough. There had been no bleeding of the gums, no nosebleed or bleeding elsewhere since the illness came on. The mucous membranes were free; there was nothing in the throat.

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[2] Dr. Head made an extensive report on the skin condition which agreed with my description of the skin tumors.

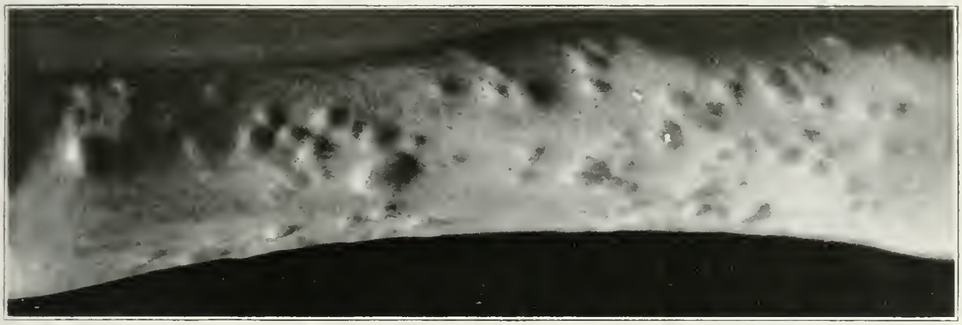

Fig. 3.—Lymphadenotic tumors on forearm: the large tumor is the primary lesion.

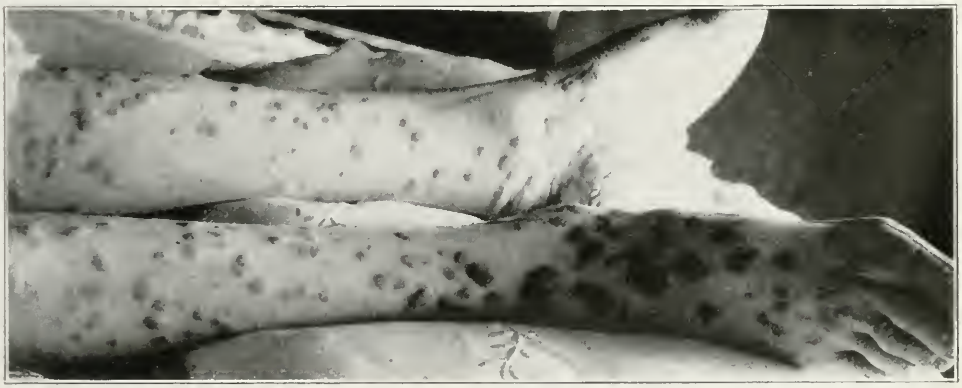

Fig. 4.—Lymphadenotic tumors on lower extremities, showing the hemorrhagic borders of tumors on the foot.

Dr. Head, Dr. S. Marx White and Dr. Robert J. Rizer kindly made blood examinations in this case at different times which were very interesting. The Wassermann reaction was negative. Their findings are recorded in the accompanying table.

A small vertical section was cut out from a nodule, fixed immediately in Zenker's fluid and examined by Prof. E. T. Bell, in the pathologic department of the university. The tissue was embedded in paraffin and the sections were stained with hematoxylin and eosin.

Under low magnification (Fig. 1) the deeper part of the dermis and a thick layer of the underlying subcutaneous areolar tissue were seen to be densely infiltrated with cells of a lymphatic type. In the deeper parts of the nodule, the cells often were arranged in large nests; in the parts nearer the epidermis, they were usually arranged in small nests or cords. A dense fibrous connective tissue separated the groups of cells. The cellular infiltration did not involve the superficial part of the dermis.

When examined under high magnification (Fig. 2), the cell nests were found to be composed of closely packed cells of lymphatic type. The nuclei were spherical or ellipsoidal and contained considerable chromatin. There was an abundant cytoplasm. Where the cells were closely packed, no cell boundaries were visible, but where they were less crowded all cells were distinct. In some areas, mitotic figures were frequently observed. The cells were of the type commonly found in organs, such as the liver and kidneys, in cases of lymphatic leukemia. The presence of mitotic figures indicated that cell multiplication had taken place in these foci.

Clinical Course.—The patient became ill first on April 14, and died, September 17. She was confined to her bed permanently after June 18. Her pulse ranged between 105 and 120 throughout her illness. She had no hemorrhages during her illness. Her chief complaint was a constant diarrhea, which persisted after the withdrawal of arsenic. Her appetite was very poor, and milk was the most suitable and sustaining food she could take. The tumors caused her no inconvenience; none of them ulcerated and there was no itching. The urine was normal except for a great increase in uric acid in the later stages. Two weeks before death, she became deaf in the right ear. She became comatose on the evening of September 16, and died the following morning. It was extremely unfortunate that a necropsy was not permitted.

COMMENT

It is hardly within the scope of this paper to speculate on the cause of lymphatic leukemia. The history and course of this case surely suggest an acute infection. It is generally understood that the bone marrow is the starting point of the disease, but in a case like this we must consider whether the lymphocytic collections which make up the tumors were manufactured in the bone marrow and deposited in the skin by the blood, or whether the skin could of itself manufacture lymphocytes at the expense of its own lymphatic centers. Admitting in this case that the bone marrow was primarily involved, would it argue against an independent lymphatic hyperplasia in the skin? If the skin infiltrations were bone marrow lymphocytes, why should the blood picture be normal up to the time, and even after the time, that all of the skin tumors had formed?

Another point worthy of careful consideration in this case was the apparent lack of involvement of other tissues and organs than the skin, during both the aleukemic and leukemic stage of the disease.

The occurrence of numerous mitoses in the lymphocyte nests argue for the local proliferation of the tumors. If we concede in this case that the primary changes took place in the bone marrow, it would not alter the fact that there is an independent lymphatic hyperplasia in the skin.

These facts would suggest that the skin may of itself undergo lymphoid transformation which would be contributory to the development of a lymphatic leukemia.

DISCUSSION ON PAPERS OF DRS. FOX AND BUTLER

Dr. **Wile** expressed his appreciation of Dr. Butler's paper because he was more particularly interested in that. He had under his care at present a most extraordinary case of lymphatic leukemia which, except for one other, was a unique case. Dr. Engman had seen the patient and could substantiate the diagnosis. The patient's disorder started with a simple exfoliative dermatitis six years before admission to the hospital, and he had been treated for eczema. This was followed by a marked pruritus. The skin began to exfoliate in 1916 at which time he had been given a dose of arsphenamin, which made the exfoliation worse. The man entered the hospital in 1919, and a diagnosis of desquamative dermatitis was made, there being no other sign of trouble. Shortly after his entrance, he developed a lymphatic enlargement, which was so pronounced that it could not be associated with the skin primarily. The blood picture up to the time of the lymph gland involvement was negative. It then revealed a very marked lymphocytosis, with a great preponderance of lymphocytic cells. The patient now presented the picture of lymphocytic leukemia. Dr. Wile was inclined to believe that the exfoliative condition may have acted as an insult which produced a condition simulating lymphocytic leukemia in the blood. Later the true picture of lymphatic leukemia appeared, with enormous enlargement of the liver and spleen, and now large nodes had developed on the skin.

There are two types of cases which one encounters: In one, as in Dr. Butler's case, there was the true primary leukemia of the skin, and in the other, to which Dr. Wile's case belonged and perhaps that of Nikolai, they were dealing with some insult to the skin with so-called secondary leukemia. His patient had received arsenic with absolutely no benefit to the condition, and he was also febrile.

Dr. Wile showed photographs of his patient.

Dr. Wile stated that the histologic sections taken from four different parts were studied and showed a typical picture of lymphatic leukemia, as did also an excised gland.

Dr. **Wende** stated that he believed that as shown by the photographs, one of his patients, aged 64, had lesions corresponding to the type described by Dr. Butler. The lesions were distributed over the entire body and although the patient was not continuously under his care the lesions seemed to conform to those in Dr. Butler's case.

Dr. Wende referred to his publication in the *American Journal of the Medical Sciences* in 1901, of the report of a case of lymphatic leukemia developing from a case of Hodgkin's disease and culminating in streptococcus infection. In this case the lesions corresponded to those in the case of leukemia just reported by Dr Butler and also to those in the case of Hodgkin's disease just reported by Dr. Fox. Dr. Wende stated that he then (1901) directed attention to the indefinite and unsatisfactory classification of lymphosarcoma and pseudoleukemia; and that there was a possibility of an aleukemic stage preceding a true leukemia. The presentation today of the two dissimilar cases with such similar tumor lesions had again brought the contention of that time to the fore. Nevertheless, from the pathologic findings in his case and in that of Dr. Fox he did not think that they were in any way allied. His own case, when the patient was first seen, corresponded clinically to Hodgkin's disease, but the tumors were due mostly to lymphocytes that he then stated, and that he still believed, escaped into the skin through rents in the blood vessels, which opinion was subsequently concurred in by Walsh and others. The patient had typical nodular infiltrates, and when the condition developed into acute leukemia it presented other manifestations such as the generalized purpura, the itching and many of the other manifestations referred to by Dr. Fox.

Dr. Wende expressed his appreciation of the privilege of hearing the papers of Drs. Fox and Butler because taken in connection with the case reported in 1901, the clinical pictures presented by all three were so very similar that they led to the false impression that they were but different manifestations of the same etiologic factors; however, the morphology in each of the cases positively determined that they were of different entities.

Dr. Fordyce said the cases so carefully reported by the authors will undoubtedly help to give us a clearer idea of the skin conditions connected with the blood making organs. It was not so difficult to diagnose the skin changes when they occurred with the blood picture of leukemia. In the undeveloped leukemic state it was very difficult to correlate the skin condition with that disease unless repeated examinations were made, as had been made by Dr. Butler. He had at present under his observation a number of patients with generalized thickening of the skin associated with enlargement of the inguinal and axillary lymph nodes. In two of these cases a moderate leukocytosis with a relatively high lymphocytosis was present while in the third no blood change was found. How are we to classify such cases? Is the leukocytosis and associated lymph node enlargement due solely to the generalized skin inflammation or are both conditions due to an underlying disturbance of the hematopoietic system? He believed only prolonged observation with repeated blood examinations could elucidate this problem. It seemed to him important to restudy the entire group of erythrodermias and their relationship to the blood forming organs.

Dr. Grindon was interested in Dr. Butler's case because it vividly brought to mind a case of lymphatic leukemia which he observed many years ago, when he did not have the training necessary either to investigate the case as it should have been investigated, or to appreciate what he saw. Later the true nature of the case became very evident. The patient was 62 years of age and had always enjoyed perfect health. The disease began with pruritus chiefly about the scalp and face, so that the patient in seeking to relieve it acquired the habit of pulling out the hair of his beard and scalp, producing bald areas here and there. The pruritus later extended over the entire surface. The earliest portion to be involved was the face, and the lesions here remained throughout more marked than on other parts, although they were generally distributed. There was marked leontiasis; the skin about the forehead and face was thrown into thickened folds. Tumors of various sizes developed, some of them discernible only on palpation, others that could be seen and were generally discolored. Some were pink or red while others changed to a yellow or brownish hue, or even a light hemorrhagic tone. In places on the face were masses as big as a silver dollar, soft to the touch and depressed in the center. On the body were also numerous lesions, some that could be felt only, others that could be seen but that were without discoloration. Others were of a variety of colors, but there was not the play of color on the body that was present on the face. Some of the body lesions would become as large as a hen's egg or larger. There was enlargement of the lymph nodes, more particularly the axillary and inguinal, but also at other points. One characteristic of these lymph node enlargements was their great hardness. The pruritus was most distressing—as bad as in mycosis fungoides. A striking picture of the case was the change which it underwent, both as to individual lesions and as a whole. The lesions would grow to a good size and then flatten out, leaving little discoloration. Later, new lesions would come up at the same or other sites. The case went through a great variety of changes. At one time the lesions would suddenly disappear, to reappear after a few days. Again marked anemia developed for a time. The patient lived for thirteen years and died of an intercurrent disease. For some time before death, he was much improved, under practically no treatment.

Dr. Highman said that these two papers had brought to the fore once more one of the most interesting phases of dermatology, namely, the need for remaining good internists as well as dermatologists. In leukemia cutis one might know what he was talking about in the leukemic stage, but in the aleukemic, or subleukemic phases of the disease one was immediately confronted by the relationship with mycosis fungoides and Hodgkin's disease. Hodgkin's disease was very closely allied to mycosis, particularly mycosis d'emblée as Dr. Fox pointed out. There were six very important works on this subject, three by Europeans, Paltauf, Audry and Arndt, and three by Americans, Hazen, Cole and Frazer. It seemed to him that for the time being one had to be very conservative about mycosis in relation to leukemia and Hodgkin's disease. Dr. Fox's case was unique in that while it was not the first case of cutaneous Hodgkin's disease on record, he thought it was the only case in which Dorothy Reed cells had been found in the skin. In the gland section he could not find nearly so much evidence of Hodgkin's as in the skin, although the gland studied in Schenectady showed Hodgkin's disease. He examined a series of slides of Hodgkin's glands, and it seemed that the longer the duration of the disease, the less characteristic were the gland lesions, although one could always find some Dorothy Reed cells.

Dr. Highman thought it would be necessary to consider leukemia as a disease of an entirely unknown origin, inasmuch as some forms develop that act just like an acute infectious disease with hemorrhages in the skin and fever.

Dr. Hazen said that there were five conditions which were sometimes confused with Hodgkin's disease: in the first place, tuberculosis, which could be excluded; in the second place, lymphosarcomatosis, which may or may not be like Hodgkin's; in the third place, cases that may be preleukemia or aleukemia; in the fourth place, what may be simple lymphomas, as described by Warthin, and the last, those with Dorothy Reed bodies, true Hodgkin's disease. The cases with preleukemic or aleukemic conditions have been recorded more often by dermatologists than by hematologists and internists combined. The question was whether there was some traction which took those cells out of the blood and caused them to be deposited in the skin. In regard to the blood findings that were supposed to be typical, we should be very skeptical. He had seen one case in which three blood smears were taken on the same day and sent to different pathologists. Bunting reported more than any other pathologist could find. Tumors were taken out and found to be typically tuberculous. One thing about mycosis fungoides to which Dr. Highman originally called his attention was rather interesting. That was that at first there is apparently a generalized stage similar to leprosy and syphilis, and then fewer but ulcerative lesions. In the leukemias there were two classes: the first, the acute cases with the marks of an infection in which the leukocytes do not exceed from ten to fifteen thousand, and if there is any increase in lymphocytes it is principally of the large varieties; the second, the chronic cases with the increased small lymphocyte counts. Between these two are various stages in all of which it is impossible to tell whether one is dealing with the acute or chronic stage. Dr. Hazen called attention to the work of Türck who had emphasized all this and pointed out that the disease might change from the aleukemic to the leukemic stage and might occur within a short interval. The whole subject was fraught with difficulty at the present time.

Dr. Hazen was very glad to have heard both of these reports, and said they were cases that had been admirably worked up.

Dr. Hartzell believed we should distinguish between true leukemic conditions of the skin and toxic eruptions occurring in leukemic subjects. In one case under his observation recently in which there was a leukocytosis of 130,000 with 70 per cent., or even higher, of lymphocytes, there had been a continuous eruption which was most abundant over the buttocks, the thighs and in the popliteal spaces, which in the first twenty-four hours looked much like the wheals of urticaria. Later, some of the lesions became hemorrhagic; at times there were bullae on the forearms. After the lesions had existed for a few days, they resembled the large, flat papules occasionally seen in erythema multiforme. There was no itching except in cold weather when there was moderately severe pruritus. Sections made of these lesions had shown very little histologic change. There was a very scanty perivascular exudate and some edema. There was no infiltration of the skin with lymphocytes; here one had to do with a toxic eruption. The patient was given benzol, with no benefit, but radiotherapy produced an enormous improvement in the blood count but none in the patient. When the patient was seen within a month or two, he had only 7,000 white cells, but the relative proportions of the cells in the differential count remained about the same.

Professor Lindenberg said he considered leprosy very similar in appearance to leukemia. He had a case in which there were spots all over the body which were not anesthetic. In the histologic examination they found giant cells, which was very rare in leprosy, so they believed the case was one of mycosis fungoides. A year later he saw the patient again and found that the spots had enlarged and become anesthetic in the center. He then thought it was leprosy and found the organism in great quantities in the lesions. This was undoubtedly a case of leprosy which seemed very like mycosis fungoides in the beginning.

Dr. Cole was much interested in both of these papers for each case seemed unusual. He believed Dr. Fox's case was one of true Hodgkin's disease or lymphogranulomatosis involving the skin and considered it a pity that internists were not more interested in the cutaneous manifestations of these diseases. Last year he went into the medical ward of a Cleveland hospital and found a case of lymphatic leukemia with quite marked skin infiltration. Recently he found two cases of Hodgkin's disease side by side in a hospital, one with a very nice prurigo-like exanthem. These cases were closely related; he had seen transitions forward and back. If the Association made a careful survey and reported yearly on these cases, light might possibly be thrown on the matter and a definite advance might be made as to the etiology of the conditions.

Dr. Stokes said that two recent textbooks contained an illustration of leukemia cutis taken from a patient who later came under his observation. This patient had died of Hodgkin's disease. If anyone used the picture again he believed it would be worth while to state that while the picture did resemble leukemia cutis the patient died of true Hodgkin's disease.

Dr. Stokes said it was a pity that some mention of therapy should not be made. Dr. Cole had brought out a valuable point that internists should be stimulated to recognize the early cutaneous symptoms particularly of Hodgkin's disease. He thought it a crime for anyone to see a dermatitis with intense pruritus and not investigate the glands and find out whether the patient had Hodgkin's disease or lymphosarcoma. Enormous doses of radium had radically modified the prognosis of Hodgkin's disease, and for a clinician to go up and down a ward, time and time again, overlooking the possible meaning of generalized pruritus and early exfoliative erythrodermias was to condemn to death patients who might have had considerable prolongation of life, if not cure, with early diagnosis. In the roentgen-ray examination of the thorax in patients who were suspected of having Hodgkin's disease it was essential to realize that mediastinal masses in Hodgkin's disease were not always visible. In his patient the mediastinum was absolutely solid, but the roentgenogram revealed nothing but lateral displacement of the mediastinal tissue, due to a collapse of the lung, secondary to hydrothorax from lymphatic stasis.

Dr. Pollitzer said that he had seen Dr. Fox's patient and the slides and that he believed there was no doubt that it was a true case of Hodgkin's disease with lesions in the skin. Two points were of particular interest: first, in his experience, the value of treatment with roentgen rays. He had had for the last two years a patient with leukemia whose sole lesions were of the urticarial, vesicular and occasionally bullous and hemorrhagic-bullous type. The eruption was definitely controlled to the extent of complete freedom from any lesions for many months at a time by systematic radiotherapy directed to the enlarged lymphatic glands.

The second point of interest was the great frequency with which lesions of the tonsils were mentioned; apparently infections of the tonsils which sometimes preceded for many months the first appearance of any lesions which would suggest a diagnosis of leukemia.

Dr. Engman said it was very interesting to follow the relationship between the experimental animal tumors, especially those of the dog, and the so-called sarcoma. The trouble is that they are all morphologists and are splitting hairs on the morphologic appearances of tumors or eruptions, and not studying what is back of them. This group is much confused, and no one can entirely differentiate them. He had had an opportunity to study a comparatively large number of cases of mycosis fungoides and leukemia cutis and a few cases of Hodgkin's disease with eruptions. It appealed to him that leukemia of the skin was a distinct entity and did not change its morphologic appearances like some others which were mistakenly put in this group. Maud Slye's studies of mice cancers, in which some strains would run carcinomas and some leukemia, were interesting from this standpoint. It is very possible that some stimulus might incite the growth of blood cells in one person and epithelial cells in other persons. At the Skin and Cancer Hospital they had several times encountered carcinoma and sarcoma in the same person. In the group, the stimulus, whatever it is, whether micro-organism or chemical change that causes the growth of these cells, might stimulate one group of cells or another, and the question might hinge on one of localization of cell stimulation. Leukemia, as Warthin and Dock have pointed out, might begin in the skin or in another portion of the body with a secondary blood picture. In postmortem appearances, mycosis fungoides and leukemia differ widely. In one case of leukemia where the first symptom occurred as a small tumor on the forehead, the postmortem changes showed involvement throughout all the viscera. Mycosis fungoides never showed a blood picture anything like that of leukemia; and Hodgkin's disease may also be differentiated in this way. Dr. Engman believed the thing that should be done was to generalize more, and not to split morphologic hairs.

Dr. Howard Fox in closing, said it was a great pleasure to have heard the very interesting and pertinent discussion on these two papers. It was a great personal satisfaction to him to have had the diagnosis, in his case, concurred in by those who had given special study to this particular subject.

He believed that very little progress in differentiating Hodgkin's disease and mycosis fungoides would be made until the causes of these diseases were determined. None of the work along these lines was conclusive, including that of Bunting and Yates, and the etiology of Hodgkin's disease still remained unknown.

In answer to one of the speakers he said that his own case was not unique in showing the presence of so-called Sternberg or Dorothy Reed cells, but that in the few reports of cases quoted in his paper, these cells had been found.

Dr. Butler, in closing, said he was very much pleased with the admirable discussions of these two papers. A point of interest was that in both the tumor and universal forms of leukemia cutis the histologic picture showed similar alterations but that one form never went over into the other. In looking over the literature he found that in cases of the universal form the skin sections showed numerous mitoses, whereas, in the tumor form they were rarely observed, this case being an exception in that mitoses were numerous.

XVI.—SOME STUDIES ON LICHEN PLANUS

BASED ON THE STUDY OF ONE HUNDRED AND SEVENTY-NINE CASES *

FRED M. JACOB, M.D.
ST. LOUIS

The literature on lichen planus is large but, except for a very few phases, the entire condition is still open to discussion. The papers by Little and White read before the American Dermatological Association and the discussion which followed included the opinions of many dermatologists on this condition. All agreed as to its typical histologic picture and its usually typical but sometimes multiform clinical manifestations. This multiformity was well demonstrated by Fordyce and MacKee in a series of photographs and in their accompanying discussion.

The etiology, symptoms, course and treatment of lichen planus has caused much and diverse comment. Starting with the early writers we find controversy as to whether its cause is microbic or neurotic. Most of these believed in the neurotic etiology though the histologic picture led some to infer it was infective. Lassar claimed to have demonstrated a bacillus in the lymph spaces of the corium, but this finding was never corroborated, so that the belief that lichen planus was a neurosis gradually gained ground. Of late, however, many men have expressed doubt concerning this theory. Engman and Mook quoted several cases and advanced some arguments in favor of the microbic theory. They also called attention to the granulomatous character of the lesion. In the discussion mentioned in the foregoing, Hartzell, Pusey, Trimble, Pollitzer, Lieberthal, Mitchell and Gilchrist all expressed the opinion that the condition was an infective one. On the other hand, a number of men are of the opinion that the theory of the nervous or functional origin of the condition has by no means been disproved.

The course of both treated and untreated cases varies considerably. Little cites one case in which the condition had existed fourteen

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* Studies, reports and observations from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

years before the patient sought the advice of a physician. Fordyce and MacKee believe that the disease is self-limited and that in most cases it will disappear within a year whether treated or not. The most pessimestic view as to prognosis is found in Tilbury Fox's textbook. He states that in some cases marasmus and death would be the outcome. In treated cases the course varies considerably as also does the treatment in the hands of different men, and variations are likewise found in the records of symptoms, both local and constitutional.

The following series of cases is presented principally as a statistical study and also for the interest there may be in their histories and the results of their treatment. These case reports were taken from the records of the Barnard Free Skin and Cancer Hospital, Washington University Dispensary, and from the private files of Drs. Engman and Mook; the treatment was the routine followed in these places. The great majority of the cases were definite, usually quite typical examples of lichen planus, while in a few atypical cases the final diagnosis was reached after thorough study. As many of these cases were referred for diagnosis only, and others were referred for a single exhibition to the students, the histories of a few are not as complete as one could wish, thus making it impossible to have absolutely accurate figures in the statistical tables, and apologies are offered for any slight discrepancies which may be present.

The total number of cases was 179, of which 121 were seen in the clinic and 58 in private practice. The percentage of incidence approximates 1.25 per cent., which is in accord with the findings in other series. There were 110 females and 69 males, which shows the usual predominance of the condition in women. The majority of the women were housewives and very few of the others were engaged in hard labor. Several farmers, an engineer, a huckster and a few others were engaged in outdoor work, but most of the patients were employed as clerks or in some indoor capacity. All statistics on this disease show that it is far more prone to affect indoor or mental workers rather than those engaged in outdoor or manual occupations.

Only five negroes are presented in this series, which is a small number when one considers the large numbers of negroes who attend these clinics. However, the negro does not seem to be frequently affected, for neither Little nor White refer to a case in a negro, while Gilchrist says that possibly only half a dozen cases were recorded in the Johns Hopkins Dispensary in the last twenty years. The eruption in the negro is typical in every respect except in color, which depends a great deal on the degree of pigmentation of the patient's skin. The very dark skins show a grayish papule which has a typical morphology.

The duration of the eruption before the patient presented himself for treatment varied considerably in the different cases. Generalized cases were seen within a few days or weeks after the outbreak of the eruption, but in some of the localized cases the lesions were present for months or even years before the patient was seen. The cases where lesions first appeared in the mouth always had a history of long duration. In one case a lesion in the mouth was present for two years and then came to treatment only because a general eruption of papules had occurred. Another case gave a history of having had a dime-sized lesion on the outer side of the right knee for four years before other lesions appeared, while a third patient presented a hypertrophic lesion, 12 by 6 cm., on the outer side of the thigh, which had been present for nine years. Many cases had been treated, seemingly cured, and had one or more relapses, but there are in this series no records of cases which healed spontaneously.

AGE INCIDENCE

The youngest patient was a girl of 2 years, who had an eruption on the buttocks which appeared some weeks after her mother had been under treatment for this condition. The youngest hyperthropic case was in a child of 14 years. Both of these patients are somewhat younger than are usually found. The oldest patient was 77 years of age and had a case of the hypertrophic variety. In Table 1 may be found the percentage of cases, both typical and hypertrophic, which occurred in the different decades of life.

TABLE 1.—Incidence of Typical and Hypertrophic Lichen Planus at Various Ages

Decade of Life	All Types Per Cent.	Hypertrophic Per Cent.
First	2	..
Second	8	4
Third	20.3	10
Fourth	18	25
Fifth	25	20
Sixth	17	30
Seventh	7.3	7
Eighth	2.3	4

These figures show that both typical and hypertrophic cases are most frequent in the fourth, fifth and sixth decades of life. The very marked diminution in hypertrophic cases in the seventh and eighth decades cannot be accounted for, as one would expect old people to be more prone to hypertrophic lesions.

PRURITUS

The pruritus varied from an almost unbearable symptom to practically none. One localized case suffered so from pruritus that he hacked the lesions with a knife to relieve his distress.

DISTRIBUTION AND TYPE

Thirty-eight cases showed a generalized eruption of typical papules on all parts of the body, many of them having lesions on the mouth and on the penis; a very few showed face lesions and none, scalp lesions. The appearance of the papules was typical and requires no description here. Five other generalized cases exhibited, along with the usual flat papules, numerous hypertrophic lesions which differed only in their accuminate character and their lack of a flat shiny top. The remaining cases showed either a single lesion or patch of lesions, or a few scattered patches in various locations. An idea of which locations were most frequently affected, either alone or in conjunction with other parts, may be had from Table 2.

TABLE 2.—Distribution of Lesions in Other Than Generalized Cases

	Alone		With Other Parts	
Part of Body	Typical	Hypertrophic	Typical	Hypertrophic
Mouth	7	..	10	..
Face	4	..	6	..
Neck	4	..	17	..
Arms	8	1	53	2
Hands, wrists	5	3	26	2
Trunk	3	..	20	2
Thighs, buttocks	3	..	12	1
Penis	1	..	4	..
Scrotum	..	..	1	..
Anus	..	..	2	..
Legs	10	9	3	30
Feet	..	..	8	1
Fingernails	..	..	1	..

It will be noted in these figures that, though the arms and hands are by far the most frequently affected, all parts of the body are liable to the disease. The hypertrophic variety is most often seen on the lower extremities though occasionally other parts are affected.

VARIATIONS IN TYPE

Numerous peculiarities were seen in the localized cases. A few were linear and seemed to follow the course of certain nerves while two linear cases showed a moniliform arrangement. These linear cases were so few in number as to have no particular significance.

There were rather frequent examples of the circinate and annular type of lesions, which were composed of slightly hypertrophic papules but did not differ in other respects from the ordinary cases.

Six cases showed small or medium sized vesicles, as well as papules, and in two cases these vesicles were located on the soles.

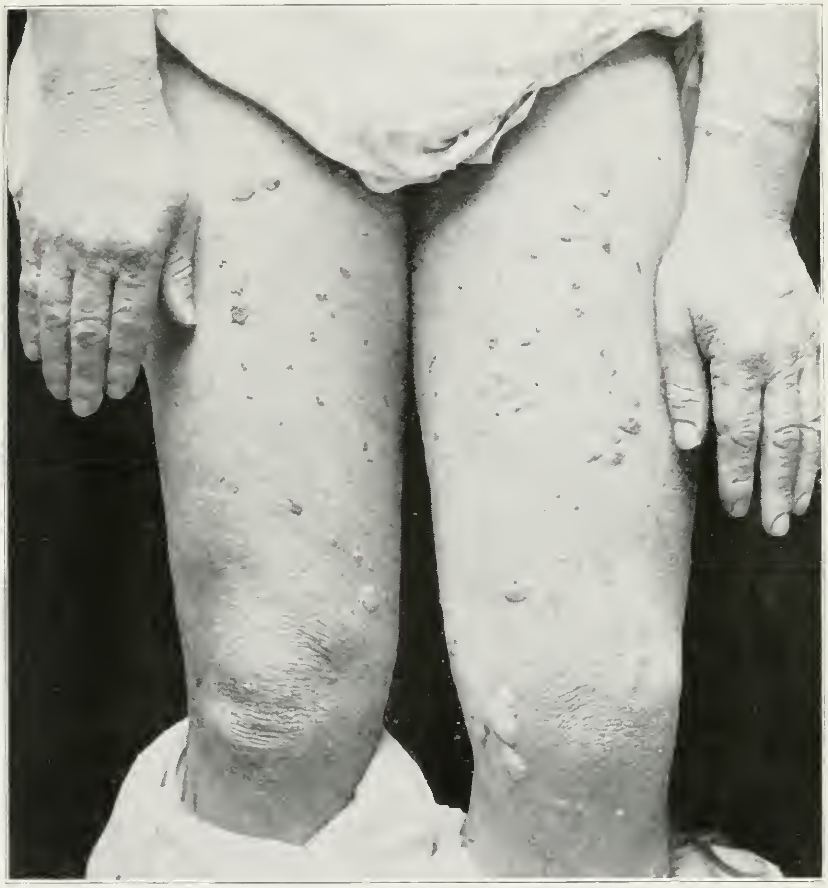

Fig. 1.—Bullous lichen planus.

One case (Fig. 1) had several crops of large bullae, chiefly on the thighs and arms, while another showed bullae on the arms and neck.

The single case of involvement of the nail showed a scaly brownish line several millimeters wide which extended along the midline of the thumb nail.

Another patient (Fig. 2) showed on the thighs a number of well-marked plane papules in and around typical plaques of pityriasis rosea. The lichen planus lesions had been present for some time when the acute outbreak of pityriasis rosea occurred.

The lesions in the mouth varied in size from that of a pinhead papule to elevated plaques covering large areas of the cheeks or tongue. Figure 3 shows some lesions on the buccal mucosa located among very pronounced lesions of Fordyce's disease.

DISCUSSION

A careful study of the more complete histories of this series gives practically no positive evidence as to either the nervous or infectious origin of this condition and any interpretation of the cases is most difficult. In a small number of cases severe nervous shocks occurred before the eruption, but these were so few in number that they can be considered as coincidences. Other patients denied any possibility of nervous shock or worry of any kind. Drs. Engman and Mook in a previous publication have reported some of these cases and have also mentioned several other cases of this series that seem to show the infective character of the disease. In their discussion they also bring out the fact that many of the patients have distinct constitutional symptoms and are far more nervous and irritable than the pruritus would warrant. They believe that this may be a sign of a generalized

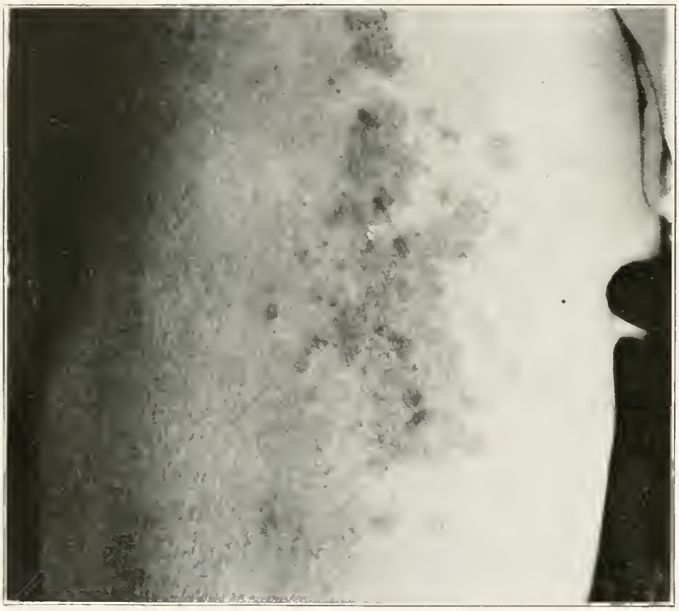

Fig. 2.—Pityriasis rosea and lichen planus.

infective process of which the eruption is the outward manifestation. In this light it may be interesting to compare some characteristics of lichen planus with a number of definitely toxic or microbic conditions.

A number of these cases show a beginning in a primary single lesion and some in a single small patch of lesions. The general eruption appeared only after a varying incubation period. A few of these cases showed toxemic symptoms accompanying the rash. These characteristics are comparable to the primary and early manifestations of syphilis. The old hypertrophic lesions which remain long after the acute attack subsides are to a certain degree comparable to late manifestations of syphilis, while the response of both conditions to arsenic and mercury is quite striking. The appearance of lesions at points of irritation is another well known characteristic of lichen planus which is also present in a number of diseases that are definitely toxemic or microbic in origin. Syphilis, erythema multiforme, dermatitis medicamentosa and the acute exanthems all show this characteristic. As all these conditions are indefinitely due to some toxin or micro-organism present in the blood stream, this similarity would seem to be of some significance. The histology of the lesion also suggests a microbic rather than a nervous process. All observers agree as to its granulomatous character. Its rather slow progress also seems to be more that of a microbic infection than a trophic disturbance.

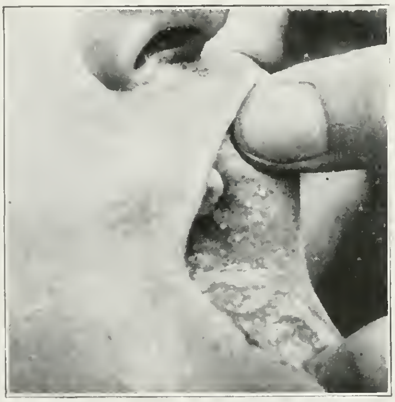

Fig. 3.—Buccal lichen planus and Fordyce's disease.

It is hard to find a trophic disturbance producing a lesion with the histologic character of lichen planus. On the other hand, one can show lesions analogous to lichen planus caused by infection. The various clinical types of lesions in the lichen planus group may very well depend on the anatomic localization of the irritant (virus?). If it is follicular we have the accuminate lesion with the horny and ob-

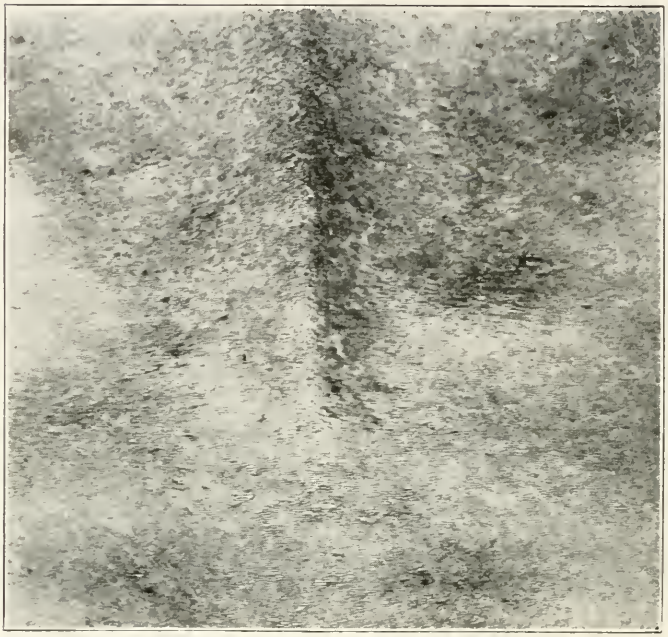

Fig. 4.—Circinate scars following lichen planus.

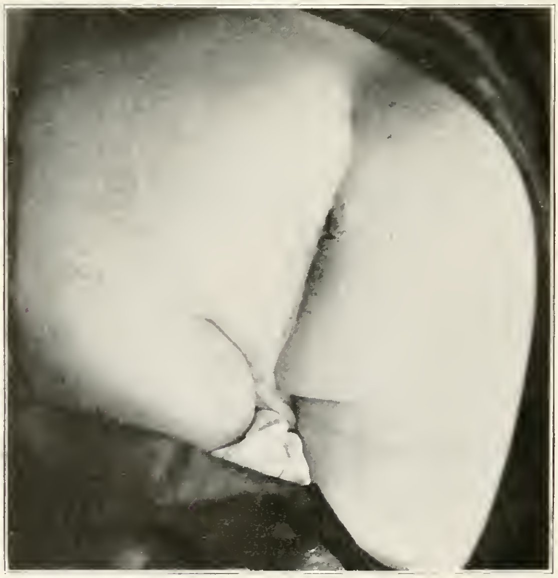

Fig. 5.—Lichen planus in a child 2 years old.

tuse papule. If it is in the upper part of the dermis without a localization particularly related to an anatomic structure, it may be a plain papule. Under certain unknown conditions horny concretions may occur about a follicular localization, producing umbilication when the horn is desquamated. The color, as in syphilis, depends on the localization and the relative proportion of typical lichen planus cells. Patches are formed by the close localization of the virus (?) and by the fusing of groups. It must be remembered that lichen planus is a subepidermic-corium disease; the irritant or virus apparently finding a favorable habitat in the succulent lymph area just under the epidermis in the

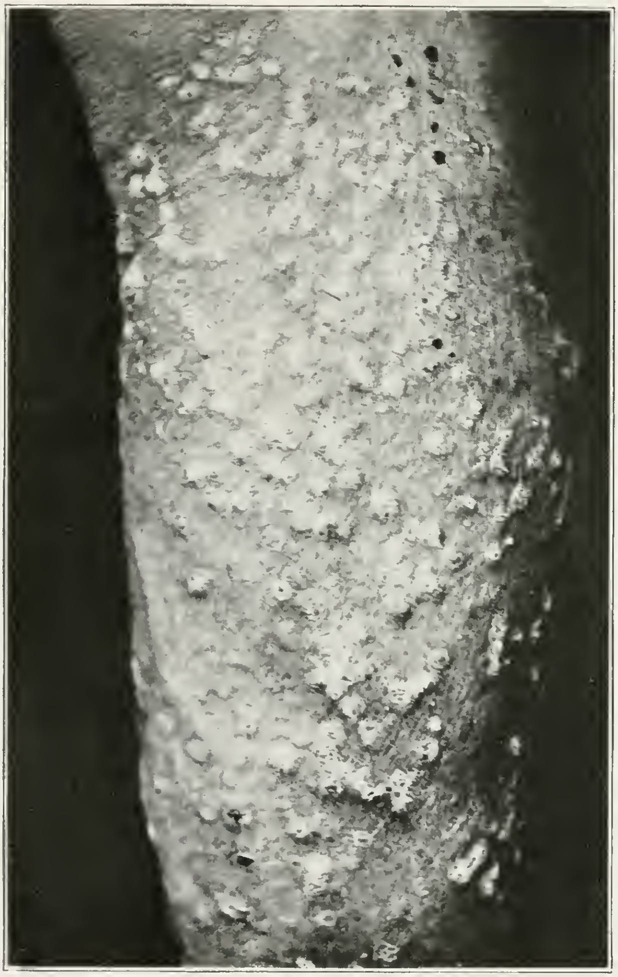

Fig. 6.—Marked hypertrophic lichen planus.

upper part of the corium. Mild epithelial edema in this region is always a cause of pruritus. The hypertrophic lesion seems to be from histologic study a question of anatomic localization and soil, as some individuals seem to be prone to the hypertrophic form of lesion. The annular lesion, as in syphilis, can only be explained by the resistance of the tissues to the invasion of the virus, with rapid repair and peripheral extension of the proliferating invader. Sometimes restitutio ad integrum is not accomplished and superficial scars result, as in the atrophic type and in another type in which the skin seems to return to normal and regains its color except for leaving a minute cicatrix at the point of the former lesion (Fig. 4).

All of these points materially strengthen one's opinion of the microbic origin of the disease. The localization of the virus and the general symptoms of invasion in the acute cases cannot be analyzed on any other known etiologic basis; such conclusion conforms to the known and well demonstrated ideas of systemic invasion and cutaneous localization. Whether the hypothetic virus localizes in other organs than the skin has of course not been demonstrated, with the possible exception of the bladder and the gastro-intestinal canal.

TREATMENT

In the treatment, mercury, arsenic and the roentgen ray were found to be efficient. In acute cases mercuric chlorid, either intramuscularly or by mouth, worked well. The dose started at a moderate size and gradually increased. It was noted in many cases that the symptoms of nervousness and irritability and the pruritus disappeared under mercury, some time before the eruption was influenced. In the subacute cases the protiodid of mercury or Fowler's solution were used and in practically all of these, one or the other was found to effect a cure. In the chronic cases arsenic in the form of Asiatic pill was the most efficient remedy. Some few localized hypertrophic cases of long standing which could not be cleared with any of these remedies, responded to the roentgen ray. It was noted that though the preparations of arsenic mentioned were effective under the circumstances given, arsphenamin and its derivative were of little or no value in the treatment of lichen planus.

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SPONTANEOUS GANGRENE FROM ENDARTERITIS-OBLITERANS *

AUGUSTUS RAVOGLI, M.D.
CINCINNATI

This disease occurred in a woman, 63 years of age, who had been married twice. The first husband died from aneurysm of the aorta abdominalis. During her first marriage she had had several miscarriages and one son who, at the age of 20, was tabetic. She enjoyed fairly good health until about six years ago when she had an ulcus perforans of the ball of the right foot and slight glycosuria. A mixed treatment and local application of a mercurial plaster caused the ulcer to heal, and she improved considerably. Last year she had an attack of acute pain in the foot and leg of the same side, and at the metatarsophalangeal joint a bluish spot formed, which in a few days turned into gangrene. The skin of the foot and leg was white, destitute of blood; the pulsation of the arteries, especially of the tibial, could scarcely be felt; no congestion and no phlebitis were present. The temperature of the skin of the foot and leg was below normal, the patient complaining of a cold sensation. Vision was greatly diminished in both eyes, the urine showed albumin and hyaline casts, together with some sugar. Fever, insomnia and mental depression, indicated that she was in a septicemic condition. The only hope of saving her life lay in amputation of the leg. After the operation she improved greatly, healing taking place by first intention.

Although the Wassermann test of the blood had been negative, she began treatment again with small doses of potassium iodid. From the stump a piece of the tibial artery was taken for pathologic examination.

The photomicrographs show the condition of the artery at the place of the formation of the thrombus. The intima is entirely deformed, and there is a tumor formed by small infiltrating cells in the middle of the lumen, where the blood has begun to coagulate. The artery below the thrombus is greatly deformed, the lumen is oblong with signs of canalization resulting from the efforts of Nature to force the blood through.

Apparently the rough edges of the broken intima act as factors causing the albumin and fibrin to coagulate and so to obstruct the

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

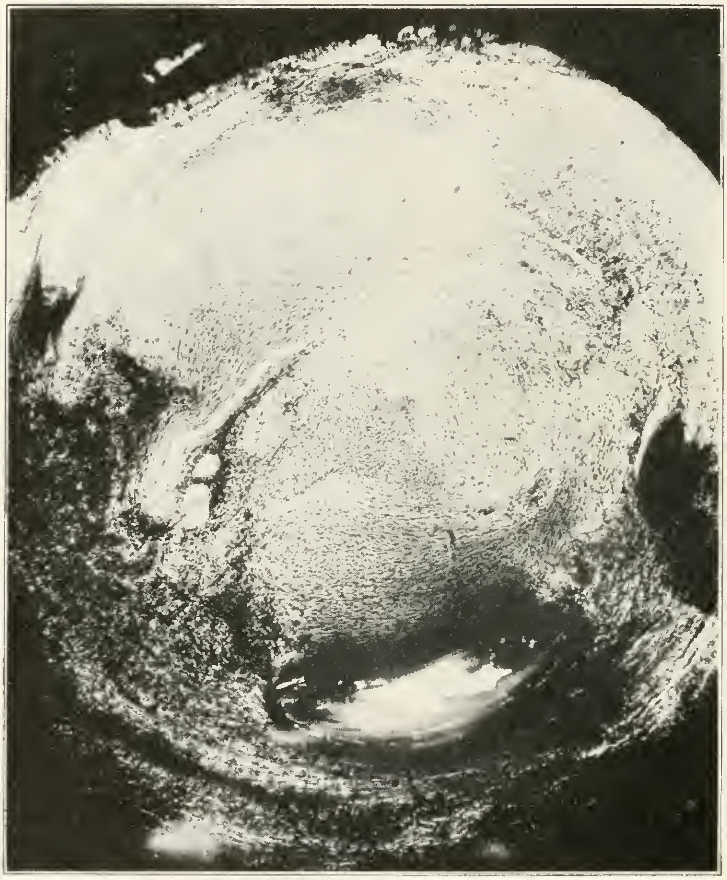

Fig. 1.—Tibial artery plugged with thrombus, a gummatous formation protruding from the media and affecting the intima; hard, thick thrombus occluding the lumen of the artery. There is a small hole on the side of the thrombus showing a tendency to canalization. (Low power.)

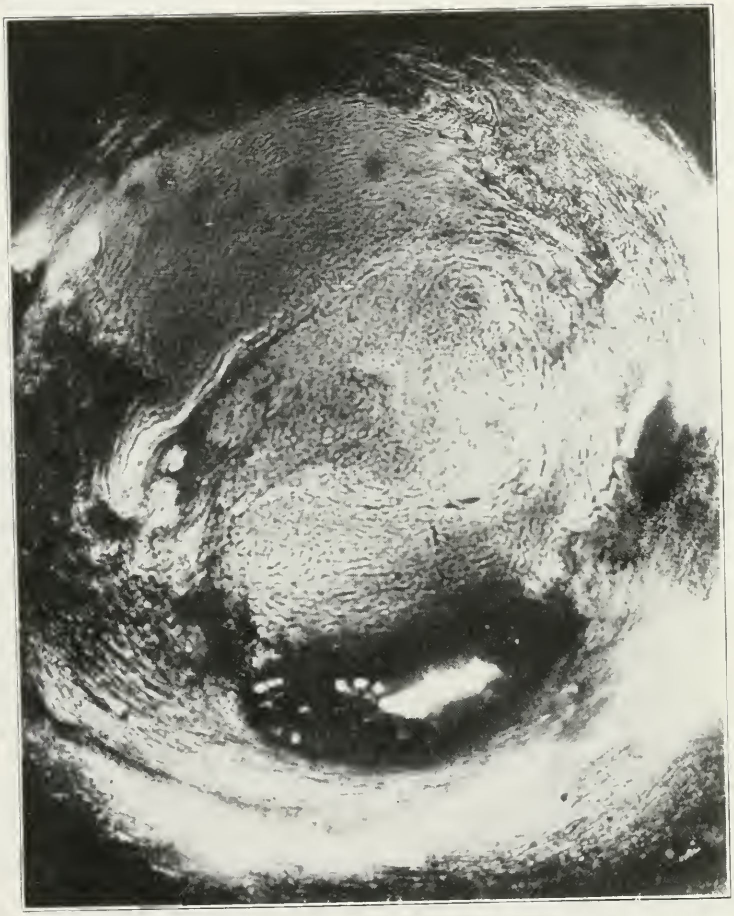

Fig. 2.—Tibial artery plugged with thrombus; a gummatous formation protruding from the media and affecting the intima; hard, thick thrombus occluding the lumen of the artery. There is a small hole on the side of the thrombus showing a tendency to canalization. (High power.)

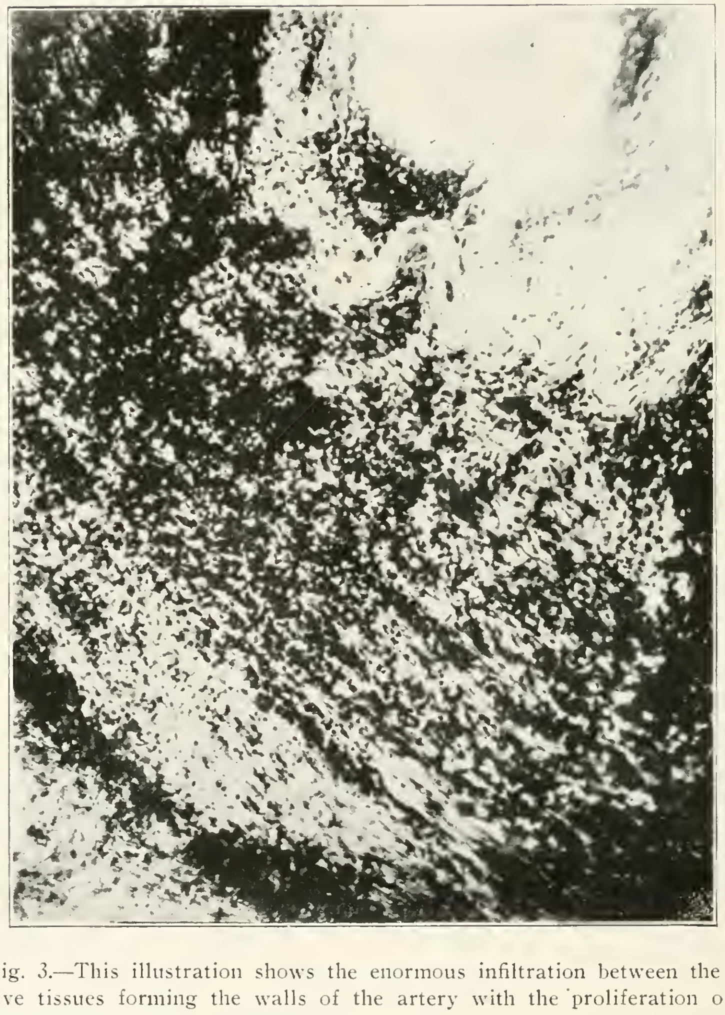

Fig. 3.—This illustration shows the enormous infiltration between the connective tissues forming the walls of the artery with the proliferation of the connective tissue fibers. (High power.)

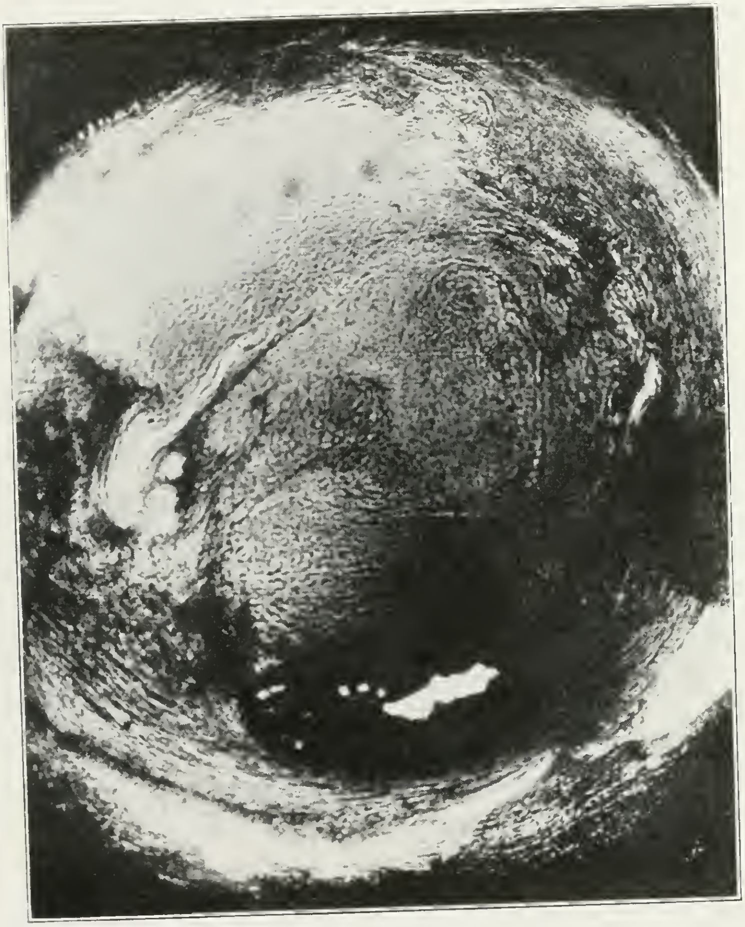

Fig. 4.—This illustration shows where the thrombus has had its origin from the breaking of the summit of the gummatous protuberance.

lumen of the bloood vessel. The whole process resembles a specific gumma which has broken the endothelium of the intima and so has produced the thrombus.

I therefore maintain that an endarteritis obliterans of specific origin exists.

Comparing the present case with thrombo-angiitis Buerger, we find that they are different conditions. Buerger's disease is a progressive one, increasing in gravity, showing more hydraulic alterations with redness, swelling, edema and plugged veins. It usually affects young persons, and apparently the immoderate use of tobacco is a factor. Buerger's disease comprehends a series of affections of the bloood and of the pressure of the blood vessels, which finally causes the formation of thrombus and gangrene. This condition can be benefited by intravenous infusion of Ringer's solution to dissolve the coagulated blood. In the present case of endarteritis obliterans, only the antisyphilitic remedies may give some relief, but there is no possibility of dissolving a hard coagulum formed from the damage of the intima by the specific gummatous process.

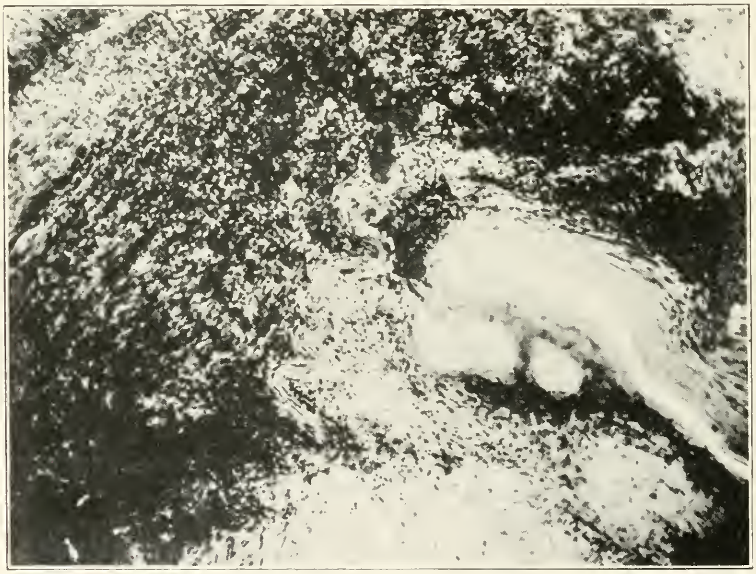

Fig. 5.—The blood vessel taken quite a distance from the origin of the thrombus. It is entirely deformed in its lumen with a small opening showing the effort made by nature to force blood through the occluded vessel.

A FATAL CASE OF RECURRENT DESQUAMATIVE SCARLATINIFORM ERYTHEMA, WITH REVIEW OF THE SYMPTOMATOLOGY AND PROBABLE ETIOLOGY *

JOSEPH GRINDON, M.D.

ST. LOUIS

REPORT OF A CASE

History.—I saw the patient on January 31 and again the next day, in consultation with Dr. N. R. Rodes of Mexico, Mo. The patient was a large, strongly built blond of 17, a student at a military academy, where he boarded. The health of his family and his previous health were good. As far as could be learned, he had not been exposed to scarlet fever.

About the middle of November last, he "broke out red all over." He did not feel more than slightly ill. He had slight sore throat and moderate fever for about two days. The eruption lasted three days, and was immediately followed by profuse furfuraceous and lamellar scaling, the epidermis coming off from the palms in large strips. There were no sequelae. The attending physician made a diagnosis of scarlet fever.

He apparently remained in perfect health until January 18, when he had a second similar attack. His temperature was 102 for the first twenty-four hours; then it dropped to 99.5, returning to normal on the third day. There were no evening exacerbations. The pulse varied from 104 to 108. There was no albuminuria. There was general redness for forty-eight hours, followed as before by desquamation.

After an interval of nine days of apparent health, except for the scaling, he had a third eruption on January 29. His temperature was 101.6 to 103. On January 30 his temperature was 103 to 104; pulse, 120 to 140. His throat was much inflamed. No albuminuria was present. January 31 his temperature was 104 to 104.6.

Examination.—At the time of my visit, the face including the lips, neck, trunk, the upper extremities including the hands, the hips and thighs, showed a bright scarlatiniform redness. On the upper part of the legs, below the knees, the eruption was rather fine punctiform, in places coalescing into a continuous erythema. The feet were free from the eruption. The palms were deep red, due to exposure of the thinned epithelium by the last desquamation, which still persisted at the borders of the hands and at scattered points elsewhere. There were no hemorrhagic striae along the elbow-flexure folds, as pointed out in scarlet fever by Lippmann of St. Louis, but both above, and more particularly below the right elbow-flexure, there were crowded pinhead petechiae.

The mucous surfaces of the soft and hard palate, pharynx, fauces, tonsils and the buccal mucosae were deep red, velvety and swollen. The tonsillar crypts were not distended. The tongue was in part covered with a thick white coat, through which showed the red fungiform papillae, as in scarlet fever, or, where this had become detached, it was smooth and bright red. There was throat pain only on attempting speech or deglutition, and even then the effort was more difficult than painful. The palpebral mucosae were deep red, the bulbar only slightly injected.

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

The lateral cervical lymph nodes were much enlarged. No other adenopathy was present. There was slight pain and tenderness about the elbows and other large joints. The bowels were slightly costive. Heart and lungs were negative. Mentality was clear.

Course of Disease.—The later history was communicated to me by Dr. Rodes. On February 1, the erythema grew lighter in hue, but again flared up for a day. On the third, jaundice appeared, which rapidly deepened, becoming quite intense. There was no nausea or vomiting, but tenderness developed over the liver and gallbladder, and became more marked over the joints. No albuminuria was present.

About midnight of the fourth, the patient became dyspneic, and from that time there was "a rapid intensifying of all mouth and throat symptoms, and intense swelling of the tongue and whole throat and neck." The dyspnea continued to recur in attacks of increasing severity, and at 2 p. m. of the fifth a surgeon, Dr. J. G. Moore, was called in to advise as to a tracheotomy.

Dr. Moore reports as follows: "At 2 p. m. the patient had extreme spasmodic dyspnea. The patient was very weak, jaundiced and evidently septic. The throat presented a sloughing appearance, but the examination was unsatisfactory, because of pain and exhaustion. The patient had just recovered from a severe attack of dyspnea. Tracheotomy was discussed, but delayed.

"At 5:30 p. m. the patient had another severe attack of dyspnea. Tracheotomy was attempted under local anesthesia. Breathing ceased under injection of procain. A rapid operation was performed, but artificial respiration proved ineffective. Some blood was found in the trachea. No membrane could be seen or felt in the larynx or trachea. Marked edema about the lower part of the larynx and vocal cords had almost obliterated the breathing space."

The following differential count was made by Dr. Jolley of Mexico on January 31: polymorphonuclears, 88 per cent.; small lymphocytes, 4 per cent.; large lymphocytes, 2 per cent.; granular eosinophils, 4 per cent.; myelocytes, 2 per cent. No postmortem examination was made.

The erythema in each attack began on the chest and arms.

LITERATURE ON THIS DISEASE

Cases of recurrent scarlatiniform erythema terminating fatally have been recorded, but in these, so far as I am aware, there were present other conditions amply accounting for death, while in this case fatality was directly due to lesions of the upper respiratory tract forming an integral part of the syndrome under consideration.

In Hallopeau and Tuffier's [1] fatal case there was rheumatism with pericarditis and albuminuria. Le Gendre's [2] post-typhoid case was not recurrent, and showed unhealed intestinal ulcers and a purulent tuberculous focus in the lung. Devic and Gardère[3] report a fatal case in which, however, the erythema was evidently but a comparatively unimportant detail added to the grave conditions which determined death, namely, arterial thrombosis due to an infection consecutive on a quiescent lung tuberculosis. The data in this case as to temperature, pulse and general symptoms are consequently not included in the summary given in the second part of this paper.

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[1] Hallopeau and Tuffier: Bull. et mém. Soc. méd. d. hôp. de Par., Series 2. **19**:221, 1882.

[2] Le Gendre: Bull. et mém. Soc. méd. d. hôp. de Par., 1893.

In reading the various textbook articles on this affection, one finds agreement as to the chief features, but more or less divergence as to some of the accompanying symptoms, some authors denying the existence of phenomena mentioned by others, and some naming symptoms as absent or mild which others say are at times severe or grave. Evidently many of these descriptions are based on incomplete information, due to the fact that the data are only to be arrived at by careful study of numerous widely scattered case reports. Even after such study of a long list of cases, it is difficult to grasp or retain the variations in symptomatology. It seemed, therefore, desirable to digest further the matter by collating the various symptoms under their proper heads so as to show their relative incidence and therefore their diagnostic value.

I have also tried to present in condensed form what has seemed probable or has been surmised as to the etiology.

Most of the facts presented are only confirmatory of what is to be found in the excellent articles by Brocq, Besnier and Doyon, Elliot, Blanc, Whitehouse, Hartzell and others. A few moot points only remain to be settled.

It may be argued that single attacks of scarlatiniform erythema are not essentially different from those that recur. As limits must be set to such an article as this, however, even though arbitrary, this form of the disease is not considered. It also seemed proper to exclude cases in which each attack was preceded by the administration of a drug, such as quinin, as in Stelwagon's well-known case, or in the second case reported by Frank.[4] This was a case of dermatitis medicamentosa, and as such falls outside the scope of this paper. The same is true of Besnier and Doyon's[5] Cases 3 and 4. It seemed, however, proper to include cases in which a first attack, following the use of a drug, internal or external, were succeeded by recurrences without such apparent cause, or cases in which some recurrences followed the use of drugs, while others did not.

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[3] Devic and Gardère: Rev. d. méd. **31**:391 (April) 1911.

[4] Frank: Jour. Cutan. & Genit.-Urin. Dis., 1897, p. 16.

[5] Besnier and Doyon: Notes to Kaposi's Treatise, Vol. 2.

Gardiner's[6] case, with a single recurrence after ten years, and "very rapid pulse," seemed doubtful, and the details too meager. I similarly exclude a case of single recurrence after eleven years, observed by me, as I could not feel sure as to the true nature of the first attack. These differ too widely from the type, with its several or many recurrences at far briefer intervals, to fit easily into it. In an intermediate position stand certain cases quoted below in which a series of recurrences was broken by a long interval only to be again resumed.

One should distinguish between recurrences and relapses, a point not brought out, so far as I am aware, in systematic articles. It is quite usual for an interval of freedom lasting over several or many months to be followed by a series of attacks separated by days only, the erythema reappearing during the desquamation following the last attack.

There seems to be general agreement on the following points, namely, that the pulse is generally slow, showing "absence of the usual relations between pulse and temperature in scarlet fever";[7] that desquamation begins much earlier than in scarlet fever, generally before disappearance of the erythema (a number of writers insist on this as a cardinal diagnostic point); that "recurrences are frequent in youth, rare in adult life, and disappear with age,"[5] although Elliot[8] says that recurrences "tend to come at shorter intervals according to the duration of the disease"; that later attacks are, as a general rule, less grave than the earlier. The fatal case here reported forms a notable exception.

Of course the number of cases in which a certain symptom is mentioned does not show the proportionate incidence of that symptom, since many reporters omit mention of some symptoms. It serves, however, to bring that symptom into greater or less prominence.

COLLATION OF SYMPTOMS

Number and Distribution of Recurrences.—In one case there were three recurrences in two years;[9] in one case, seven recurrences in two years and another after an interval of three years;[9] in one case, two recurrences in six months;[9] in one case, seven recurrences in five years at intervals of from four to eight months;[4] in one case, four recurrences in five years;[10] in one case, three recurrences in two years and four months;[11] in one case, twenty-three recurrences in

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6. Gardiner: Brit. Jour. Derm. **20**:245, 1908.
7. Blanc: Internat. Clinics, October, 1891.
8. Elliot: Med. Rec., 1891, p. 563.
9. Kramsztyk: Jahrb. f. Kinderheilk., 1902, p. 326.
10. Rotillon and Gougelet: Ann. de dermat. et syph., 1887.
11. Blanc: Jour. Cutan. & Gen.-Urin. Dis., 1893, p. 11.

eleven years and six months; [11] in one case six recurrences in one year; [5] in one case, four recurrences in two years; [12] in one case, seven recurrences in seven years; [5] in one case, five recurrences in two years and four months; [5] in one case thirteen recurrences in twenty-one months; [13] in one case, twenty recurrences; [14] in one case, 100 recurrences,[15] probably a "round number"; in one case, recurrences each spring and fall for seven years, then an eight year interval followed by another recurrence; [7] in one case, nine recurrences in four years and two months. The intervals in their order were five, two, seventeen, five, nine, one, five, four and two months. The seventh recurrence was followed by six relapses within a brief space; [16] in one case there were three recurrences in three years and eight months; the intervals were twelve, twelve and twenty months, with single relapses after the second and third recurrence.[8] In one case, four recurrences occurred in seven years and three months. The intervals were two years, four years, six months and nine months. The last recurrence was followed by two relapses.[7] In one case there were eight recurrences in two years.[17] In one case there were three recurrences in one year.[18]

Two cases are so extraordinary as to deserve repetition. Sligh [19] reports "Each year since infancy (thirty-six years), on the twenty-fourth day of July the patient has been taken ill, and within a few days thereafter, has shed the skin from the entire surface of his body, including the finger and toe nails." This occurred between 3 and 9 p. m., the acute stage lasting four or five hours. The skin came off two to four days later. Dr. Sligh observed the patient through one of these attacks. The other case, Frank's[20] recurred every year at the same date, between the ages of 7 and 33. These two cases strongly suggest a relation with the dates of flowering of plants furnishing a pollen to which the patients had become sensitized.

Intervals separating relapses (not recurrences): One week.[21] Each of four recurrences was followed by a relapse just before com-

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12. Allen: Jour. Cutan. & Gen.-Urin. Dis., 1894, p. 169.
13. Whitehouse: Twentieth Century Practice, Vol. 5.
14. Besnier and Doyon: Soc. franç. de dermat. et syph., 1895.
15. Fox, Tilbury: Diseases of the Skin, p. 258.
16. Elliot: New York M. J., 1890, p. 29.
17. Richardière: Ann. de dermat. et syph. **4**:338.
18. Petrini: Internat. Cong. de dermat. et syph., Paris, 1889.
19. Sligh: Internat. Med. Mag., June, 1893, p. 463.
20. Frank: West. M. Reporter, 1891, p. 37.
21. Billet: Bull. et mém. Soc. méd. d. hôp. de Par., April 11, 1902.

pletion of desquamation.[4] Nineteen days.[11] Three relapses within one month.[5] Seven relapses in five months.[10] A relapse within two weeks.[7]

Duration of erythema: One to six days;[22] three days;[8] four days;[7] first attack four days;[23] first four days, later one to three;[16] three days, in another case six days;[9] generally five or six days;[13] about ten days.[12]

Day of Beginning Desquamation.—Desquamation usually begins on the second or third day;[24] second or fourth day;[25] third or fourth day.[26] Desquamation usually begins before the rash has faded, say almost all who refer to this point, two noticeable exceptions being a case of Kramsztyk's [9] in which it came on only a week after the appearance of the rash, and one of Blanc's [7] in which it was delayed until "some time after the subsidence of the rash."

Duration of Desquamation.—One case lasted two, and one three weeks; the average is two to six weeks; [5] one case, two to three weeks, "many last a week or two, but more often it ceases gradually in from three weeks to two months,"[13] three to four weeks [16] or four weeks.[7]

Site of first manifestation: face, neck, upper chest; [11] one case neck, one thighs; [5] chest; [16] chest and hands; [8] some part of trunk; [27] in one case, flexures. Other writers say that first manifestations "may appear anywhere, usually not on the face;" [13] "no precise point of election." [5]

Distribution of Eruption.—In most reports in which the point is noted, the rash became universal, the feet perhaps most frequently escaping. Per contra may be placed the following: "The first attack was universal, but all subsequent ones were limited to the hands and feet." [22] "Numerous outbreaks limited to the hands and feet; [24] occasionally localized, so remaining, and ever retaining the same distribution in recurrences." [5]

Various writers note the presence of miliary vesicles, just preceding or at the commencement of desquamation.

Punctate petechiae have been noted by some as occasionally present.[28]

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[22] Elliot: Morrow's System, vol. 3.

[23] Loviat: Jour. d. mal. cutan. et syph., 1894.

[24] Bulkley: Arch. of Derm. **4**: 1878.

[25] Frank: Jour. Cutan. & Gen.-Urin. Dis., 1897, p. 16. Besnier and Doyon (Footnote 5).

[26] Whitehouse: Twentieth Century Practice, vol. 5. Elliot (Footnote 22).

[27] Hartzell: Univ. Med. Mag., August, 1895.

[28] Besnier and Doyon: Notes to Kaposi's Treatise, vol. 2. Whitehouse (Footnote 13). Elliot (Footnote 22).

Edema is sometimes seen,[29] rarely general, oftener localized,[13] as in the face,[11] and especially eyelids;[3] face and extremities.[10] Again its absence has been noted in some cases.[30]

Desquamation is sometimes accompanied by the fall of finger and toe nails;[31] while the fact of their remaining unaffected is sometimes noted.[13, 16]

Adenopathy about the head and neck was noted by Frank.[4]

Involvement of Mucous Membranes.—In this particular cases differ, as do the opinions of writers. In one of Kramsztyk's [9] patients the pharynx was uninvolved, and in the other it was reddened. Hartzell [27] says: "throat symptoms are absent or very mild." Whitehouse [13] says the throat is only slightly reddened and not swollen. Stelwagon [32] says: "the swollen fauces of scarlet fever are wanting." Besnier and Doyon [5] state that the "gums and buccal mucous membrane are often red and swollen, later with exfoliation of macerated epithelium. The nasal and palpebral mucosae are often involved." Among reported cases one finds "mucous membranes normal in every way";[16] the soft palate showed a light erythematous blush in one case; in another case "the throat ached";[7] there was erythematous pharyngitis in one case and in another, slight sore throat; in another, moderate redness of the pharynx, ulcerative stomatitis and pain on swallowing;[5] redness of pharynx;[17] tongue, fauces and pharynx showed evidences of catarrhal inflammation;[4] the mucous membrane of the roof of the mouth exfoliated in a solid mass;[11] there were sore throat, cough and hoarseness.[5]

Tongue.—The tongue is red and peeled in some cases, as in Féréol's. It may be coated, red at the tip and edges, sometimes bright red.[5] "In my cases the tongue has several times been smooth as though denuded of epidermis." [22] It may at first be coated and later peel off, leaving it clean but not red.[11] The tongue may present minute papillae at its tip and edges, but is not of the true strawberry type.[13] Some authors (Kramsztyk,[9] Whitehouse,[13] Elliot,[22] Hartzell,[27] Stelwagon [32]) especially mention the absence of the strawberry tongue.

Kidney Lesions.—Hartzell [27] says there are no kidney symptoms. Kramsztyk,[9] in three cases, reports "no visceral lesions." Frank [4] says that the absence of albuminuria is a distinguishing character. Absence of albumin is noted in a number of reports by Besnier and Doyon

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[29] Besnier and Doyon: Notes to Kaposi's Treatise, vol. 2. Elliot (Footnote 22).

[30] Blanc: International Clinics, October, 1871. Elliot (Footnote 16).

[31] Blanc: International Clinics, October, 1891; Richardière (Footnote 17); Frank (Footnote 20); Elliot (Footnote 22).

[32] Stelwagon: Diseases of the Skin, Philadelphia, W. B. Saunders Company, Ed. 8, p. 156.

(eleven cases)[5] and others (Frank,[4] Blanc,[7] Rotillon and Gougelet,[10] Blanc,[11] Allen,[12] Elliot [16] Other authors (Rossigneux,[36] Perret [33]) note its presence. It was present in Hallopeau and Tuffier's fatal case but, as before stated, it was doubtless independent of the erythema. Elliot [22] says; "Occasionally albumin may be found in the urine though it will be difficult to decide whether it is due to the erythema, or whether preexisting, or the result of some other cause." The problem just stated may at times find an answer as indicated by Devic and Gardère,[3] "One can hardly affirm that it (albuminuria) bears no relation to this affection, when it has been seen to appear with the erythema, only again to disappear." Unfortunately they furnish no references on this most essential point. In one of Whitehouse's [13] cases severe hematuria preceded each attack.

Joint Involvement.—Authors mention "arthralgia and arthropathies," [22] pain in the back, hip and knees,[7] and joint pains.[34]

Pulmonary, cardiac and pericardial affections [35] are probably only incidentally present.

Prodromes—These are apparently generally absent, although there are a few observations to the contrary. Thus the eruption has been "preceded by chills, nervousness, melancholia, dizziness and excessive sweating".[16] It has been preceded for several days by chills and fever, headache and itching of the chest and hands,[8] malaise for a day or two, then fever, headache and itching for forty-eight hours;[7] "vomiting, nervousness, restlessness, and tingling of the surface for a few days".[19]

General Symptoms.—These are generally slight, but occasionally severe: dull fever and headache were present in eleven cases;[5] headache and light fever;[7] vomiting and fever;[20] dizziness, headache, nausea and vomiting [11] are sometimes present. On the other hand, we have "symptoms of typhoid" (Féréol, quoted by Besnier and Doyon).[5] Frank says there is a condition of deep depression and exhaustion; the pulse is low and active stimulation has to be resorted to.

Pulse and Temperature.—Besnier and Doyon [5] state that "fever is almost always present, but varies widely in different cases, exceptionally it is absent." In one case it rose to 104.9. They quote Rayer, who records 100.4 and 107.6, adding that "they make a mental reservation as to the last figure, but that it at least shows the clinical use of the thermometer at the beginning of the nineteenth century."

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[33] Perret: Lyon méd., 1885.

[34] Besnier and Doyon: Notes to Kaposi's Treatise, vol. 2; Rotillon and Gougelet: Ann. de dermat. et syph., 1887.

[35] Devic and Gardère: Rev. d. méd., April, 1911. Elliot (Footnote 22).

[36] Rossigneux: Lyon méd., 1892.

The highest temperatures recorded in each case with the accompanying pulse rate are: temperature 99.8, pulse 98;[11] temperature 100, pulse 90;[16] temperature 102, in another case 103, pulse 100;[7] temperature 103, pulse 88.[20] In two infants observed the temperature was 103.4, pulse 174, and temperature 105.6, pulse 144.[9] One case showed in the first attack a temperature of 104, and in the fourth attack, a temperature of 103, pulse 120;[4] another a temperature of 105.8.[13]

Etiology.—One must almost of necessity look for a toxic cause for these phenomena. It seems equally certain that this may be any one of a widely varying series of causes. There is in no single instance anything more than a certain degree of probability as to the existence of a causal relation. It is only the absence of any constant factor, unless it be a predisposition, or condition of ready sensitization, that lends any significance to the following list of surmised causes.

Rheumatism stands out preeminently: "articular rheumatism and endocardial lesions";[10] "frequently in connection with rheumatism";[22] "acute articular rheumatism"; "rheumatic patient suffering from sciatica" (quoted from Bondet [33]); rheumatism with pericarditis.[1] Other infections are: "first attack after convalescence from puerperal fever, later repeated attacks without any assignable causes";[23] infected wound of finger;[16] true scarlet fever, two cases, and true scarlet fever and measles, one case;[9] malaria, organism found;[21] "in the ague of young children, showing the same tendency to periodic return as is seen in intermittent fever" (Cheadle, quoted by Elliot).[22] "Each recurrence preceded painful menstruation by a day or two;" in another, "at every menstrual epoch." There was an enlarged and prolapsed ovary.[16] Intermediate between this condition and dermatitis medicamentosa, and possibly pointing to a fundamental identity, is a case in which some attacks occurred after taking antipyrin or cryogen, while others were "spontaneous." [3] Both internal and external causes may be concerned in the same case, as when the first attack followed rhus dermatitis, and the second and fourth tonsillitis.[4] Among external causes are mentioned, suddenly checked perspiration;[11] chilling of surface (eleven cases); [5] cold baths (Vogler, quoted by Elliott).[16]

The variety of possible causes is emphasized by many: "Such eruptions have been seen to develop under the most various influences from the most divergent causes".[16] "Accidents precipitating the attack differ in each case".[11] Other authors say that the cause often remains undiscovered, "without any definite exciting cause"; [37] "some in which the causative influence could not be determined." [16]

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37. Besnier and Doyon: Soc. franç. de derm. et syph., 1895.

CONCLUSIONS

1. Recurrences separated by several or many months are often followed by one, or a series of relapses at intervals of a few days only.

2. The rash usually lasts three or four days, exceptionally a week or more.

3. Desquamation begins oftenest in three days, and continues two to three weeks, rarely longer. It is sometimes accompanied by falling of the nails.

4. Edema is often present, miliary vesicles sometimes, petechiae more rarely.

5. The upper respiratory mucosae are generally mildly, and rarely severely, involved. The tongue is generally coated, later peeling and red. The strawberry tongue observed in this case has not hitherto been recorded.

5. Albuminuria is rarely if ever present, unless due to some independent condition. It is possible that it may exceptionally occur.

7. The large joints are sometimes mildly involved.

8. Prodromes, febrile, gastric and nervous, continuing for a few hours or days, are present in a minority of cases.

9. General symptoms, similar to those of the prodromes, always accompany the rash. They are generally mild, but occasionally severe.

10. Fever is present at least part of the time, but is rarely high.

11. The pulse is never disproportionately high, as in scarlet fever.

12. The only constant etiologic factor lies in individual predisposition. Assigned exciting causes, covering a wide range, have oftenest been septic or toxic, although in some cases no such cause has been discovered. External causes seem occasionally to be implicated.

13. Symptoms forming an integrating part of the syndrome constituting recurrent desquamative scarlatiniform erythema may exceptionally be grave or even fatal.

DISCUSSION

Dr. Towle said that as he listened to Dr. Grindon's paper he was strongly reminded of the cases that were once called "surgical scarlet fever." They started with a wound, and developed a rash that spread outward, and there might be recurrences or a reinfection. Other cases, he had read, were due to focal infection in the sense that there was an abscess in the interior somewhere, with general toxemia.

These cases were also subject to recurrences and exacerbations. He wished Dr. Grindon had given a little more detail concerning the condition of the liver. In his opinion the symptoms pointed rather to a septic abscess in the liver producing the recurrent effects in the skin.

Dr. Hartzell thought there was little doubt but that under the term "recurrent scarlatiniform erythema" a number of diseases etiologically quite dissimilar were included. There was a group in which the symptoms were largely confined to the skin without any constitutional symptoms worthy of mention. These cases recurred year after year. In a case reported by himself several years ago the patient had suffered many attacks and had been quarantined because of the diagnosis of scarlet fever. Cases of the kind reported by Dr. Grindon certainly were the result of a marked infection of some sort.

Dr. McEwen thought this paper called attention to something that dermatologists were prone to let pass, namely, the securing of necropsies. He felt that if Dr. Grindon's case had been posted the cause of the trouble would have been found in the gall tract.

Dr. Lane said that he had recently seen a child of 5 who had had six attacks of recurrent scarlatiniform erythema in nine months. He saw the patient in the last attack, and was surprised to find that the child had a typical strawberry tongue. This was seen in none of Dr. Grindon's cases and is usually not found in this disease, its presence being indicative of scarlet fever rather than of erythema scarlatiniform.

In this case it is quite likely that the cause might have been in the tonsils, as they were hypertrophied and chronically inflamed. The physician in attendance had repeatedly urged their removal without avail, therefore nothing could be said of the prophylactic effect of this procedure. It seemed likely, however, that this case should be included in the class referred to by Dr. Fordyce.

Dr. Wallhauser agreed with Dr. Hartzell and Dr. Fordyce that many different conditions were being considered under the head of erythema scarlatiniforme, which was an extremely rare condition.

Dr. Wallhauser reported a case and showed photographs taken during the seventeenth attack. The patient was a woman, 24 years of age, who had had recurring attacks over a period of about twenty years. The initial attack occurred at the age of 5; each recurrence had a distinct onset, consisting of a feeling of malaise and depression for about one week, during which time the patient became pale and sallow. The eruption appeared abruptly all over the body, including the extremities—the face became flushed with circumorbital pallor. The onset of the eruption was accompanied by chills, followed by a rise in temperature, usually to 104 or 105 degrees; nausea and vomiting occurred during the first days of the eruption, and in some attacks was a most distressing symptom; mild or severe throat symptoms were present and painful deglutition was continuous until the disappearance of the eruption; the tongue was heavily coated, but lacked the characteristic enlargement of the papillae seen in scarlet fever. The eruption began to fade on the fourth day with a subsidence of the constitutional symptoms. Desquamation occurred, and in some attacks was complete in ten or twelve days, while in others, it was more gradual, extending over a period of four or five weeks. The photograph of the hand, showing complete glove-like exfoliation was taken at the end of the third week of the eruption.

Dr. Engman stated that Dr. Grindon had told him of this case and had reported it before the St. Louis Dermatological Society. He considered the case instructive and interesting. In his opinion there should be two distinct groups; one a seasonal condition, which might be due to pollen or any condition that might occur in certain seasons, and the large group of conditions that were septic, or toxic, in which some toxin developed from food or microorganisms.

Dr. Engman was observing a patient who had had six attacks that had been diagnosed as scarlet fever. The patient was a boy 16 or 17 years old in whom the attacks could be produced at will by quinin, but at other times they had occurred without quinin. This was analogous to dermatitis herpetiformis, in which typical attacks could be produced at will by iodid of potassium, which histologically and clinically was dermatitis herpetiformis. It seemed in Dr. Grindon's case to be some septic process.

Dr. Grindon (closing), replying to Dr. Fordyce, said that the leukocyte count was above 8,000.

The implication of the liver in this case was clear, but apparently this was not the cause of the trouble but a result. The patient was apparently in perfect health between his three attacks, and it was only after the last attack had existed for several days that any symptom developed to attract attention to the liver, such as enlargement, pain or jaundice. It was to be regretted that there had been no postmortem examination. The patient was a hundred miles from St. Louis and the local physicians were unable to secure a postmortem examination. This was, perhaps, partly due to the fact that Dr. Grindon, unfortunately, had said it was a condition with which the profession was quite familiar; that it was never fatal; and that the patient would do well.

As was so truly said by Dr. Hartzell, we are dealing with a group or syndrome, and not with a disease, etiologically; but as Dr. Wallhauser said, a condition in which there are etiologic differences, but which clinically remains true to type. It constitutes at least a clinical entity. Constancy in the duration of the erythema, in the date of beginning desquamation, and in the relation of pulse to temperature, make it useful to class these cases together and to study them under one head until more is known about them.

In studying reports of the cases and trying to separate them into groups he found a rarely broken agreement of symptoms. One thing that stands out is the distinction between recurrences and relapses. In this case there was an interval of apparent perfect health for ten weeks between the first and second attacks, so that it was difficult to believe that the same septic cause was active throughout that time. However, Dr. Grindon believed that there was a septic cause.

He was interested in hearing Dr. Lane's observation as to the strawberry tongue. So far as he could learn, this had not been recorded in any other case except the one forming the subject of this report.

The point that to him seemed diagnostic in the first attack was the absence of the characteristic disproportion between pulse and temperature so familiar in scarlet fever.

SYPHILITIC INFECTION OF THE CENTRAL NERVOUS SYSTEM OF THE RABBIT *

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Since it was first shown that rabbits were susceptible to infection with *Spirochaeta pallida,* numerous attempts have been made to devise means of producing an infection of the central nervous system in these animals which might be utilized in studying this phase of human syphilis. For the most part, the experiments which have been carried out appear to have been based on the assumption that this could not be accomplished by a simple testicular or scrotal inoculation, but that it was necessary to resort to some intensive form of inoculation, such as an intravenous, intracardial or intracranial inoculation or to the use of repeated inoculations of various kinds. This idea may be accounted for in part by the use of recently isolated strains of *Spirochaeta pallida* and in part by the apparent inability to produce a generalized disease in the rabbits by ordinary methods of inoculation.

How successful these efforts have proved it is difficult to say. The evidence of infection which has been submitted in cases other than those of direct inoculation into the cerebrospinal canal has consisted largely in the demonstration of lesions which, although analogous to certain lesions observed in man, might be produced by a variety of causes and are frequently found in rabbits which have not been inoculated with *Spirochaeta pallida.* The significance of the lesions described, therefore, has remained somewhat uncertain.

It appeared to us that, since a widespread dissemination of spirochetes always occurred in rabbits inoculated in the testicles or scrotum, whether lesions developed elsewhere or not, the first thing to be determined as an approach to the study of infections of the central nervous system was whether or not the organisms gained access to the cerebrospinal canal in ordinary types of infection and second, whether the same influences which control processes of infection in other parts of the body might not extend also to localization of the organisms in the central nervous system.

It was obvious also that the first essential in attempting to determine these facts was the use of a strain of *Spirochaeta pallida* which was as well adapted to the rabbit as possible.

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Accordingly, a small series of experiments was undertaken, the purpose of which was to determine the presence or absence of *Spirochaeta pallida* in the central nervous system at various periods of the experimental infection, more as a means of orientation than as an attempt to solve any particular problem. However, the results of these experiments throw considerable light on infection of the central nervous system in the rabbit, and for that reason may be reported in brief.

EXPERIMENTAL PRODUCTION OF SYPHILIS

The method of procedure was to obtain cerebrospinal fluid from infected animals as free from contamination with blood or tissue juices as possible and to determine the presence of spirochetes by injecting this fluid into the testicles of normal rabbits. To accomplish this, the animal was killed with ether and bled from the heart to relieve the congestion of the meningeal and other vessels. The tissues over the occipito-atlantoid membrane were then removed and the membrane scraped clean, after which a needle was inserted through the membrane and the fluid removed in fractional amounts by suction with a small syringe. In this way, an average of 0.6 to 0.8 c.c. of fluid could be obtained which was free from any visible contamination with blood.

The fluid thus obtained was examined microscopically and injected into one testicle of one or two normal rabbits, depending on the amount of fluid available. These animals were then kept under observation for a period of sixty days for the purpose of determining an infection in the testicle.

The spinal fluid of thirteen rabbits that had been inoculated in the testicles was examined by this method. Nine of these rabbits were infected with Nichols' strain of *Spirochaeta pallida* which was isolated from the cerebrospinal fluid of a neurorecidive in 1912 and four of them with an organism isolated from a mucous patch by Zinsser and Hopkins in 1913.

RESULTS

The Demonstration of Spirochetes.—The first series of animals examined consisted of five rabbits with early testicular infections. The fluid from one of these produced an orchitis after an incubation period of forty-three days in one of the two animals inoculated. Subinoculations from the others were all negative at the end of sixty days.

The successful transfer in this case came from an animal with an orchitis of eight days' duration which was produced by the Nichols strain of *Spirochaeta pallida.* There were large and actively progressing lesions in both testicles but no lesions elsewhere.

A second series of inoculations was then made from three rabbits with actively progressing generalized lesions. These gave two positive results. In one case, infection was again obtained in only one of the two subinoculations, while in the other, only one test animal was used.

One of the animals in which infection of the nervous system was proved had marked periosteal lesions with extensive necrosis of the nasal bones, which suggests the possibility of invasion of the central nervous system by way of the lymphatics. This animal was inoculated in both testicles with the Zinsser-Hopkins strain of *Spirochaeta pallida,* and the development of generalized lesions was induced by castration.

It is important to note that the incubation period of the infection produced by the spinal fluid of this animal was only thirty-six days, which is reasonably close to that of an infection produced by an inoculation with 0.5 c.c. of heavily infected blood or with an emulsion from an infected lymph node.

The other animal was inoculated in one testicle with the Nichols strain of *Spirochaeta pallida* and subsequently given a dose of 5 mg. per kilo of arsenophenyglycyl dichloro-m-aminophenol as a means of suppressing the testicular reaction. Generalized lesions were just beginning to appear and there were slight lesions of the nasal splints when the animal developed signs of a meningitis. Although the spinal fluid contained an increased number of cells, it was clear and no spirochetes could be demonstrated by dark field examination. At necropsy, no abnormality of the brain or cord could be detected beyond a possible injection of the meningeal vessels and a slight clouding of certain areas of the meninges.

The exact incubation period of the infection produced with this fluid cannot be given. The lesion in the testicle was first discovered forty-two days after inoculation, but it was then a well developed lesion of at least three or four days' duration.

The third group of animals whose spinal fluid was examined was composed of five rabbits, all of which had developed generalized lesions. At the time the examinations were made, these lesions were either regressing or had completely disappeared so that this group of cases might be classed under the head of inactive or latent infections. Inoculations from all of these animals gave negative results.

Alterations in the Spinal Fluid.—In addition to the demonstration of spirochetes in the cerebrospinal fluid of three animals, mention should also be made of the occurrence of certain obvious abnormalities in the fluid of animals when no active infection could be proved.

The striking features of these changes consisted in a slight clouding of the fluid and the presence of flocculi which on microscopic examination proved to be due to an increased number of cells and the formation of aggregates of cells and granular detritus.

These conditions were practically constant in the animals of group three, which suggests an antecedent infection in these cases with a subsequent disappearance of the spirochetes such as occurs during remissions in other forms of localized infection. This possibility is supported by the apparent frequency with which spirochetes were demonstrated during an active period of infections of an analogous character.

CONCLUSIONS

This series of experiments, although too limited to warrant any broad generalizations in regard to syphilitic infection of the central nervous system, is sufficient to show that such infections may be produced in the rabbit by an ordinary testicular inoculation of well adapted strains of *Spirochaeta pallida,* and that spirochetes may invade the central nervous system at a very early period of the infection.

How often this occurs is impossible to say since the methods used are subject to obvious limitations both as regards the type of infection which may be demonstrated in this way and the activity of the infection at the time the examination is made.

From this small series of experiments, it would appear, however, that invasion of the central nervous system by *Spirochaeta pallida* and the development of localized lesions are subject to the operation of the same set of conditions as are concerned in the occurrence of other manifestations of a generalized infection, and that by taking advantage of these conditions, it should be possible to favor this form of infection so as to increase both the incidence and severity of central nervous system involvement.

THE VANISHING LESION: A NEW PROBLEM IN TEACHING *

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Methods in teaching are not entirely beyond the influence of fashion. Changes occur in various courses that indicate the emphasis of a particular period. Class exercises give way to section teaching, with the advantage that students come in more intimate contact with both instructor and patient. Not long ago the didactic lecture seemed to be in peril of extinction. The teaching of syphilis has followed the general plan more or less closely. However, we still have a few didactic lectures and clinical exercises for the class; but the bulk of instruction is with small sections at the hospital.

Recently a new condition is confronting us: the vanishing lesions. The teacher of clinical syphilis must regard this changing condition with real apprehension. One no longer sees in the clinic the array of active lesions, both early and late, that were formerly available for teaching purposes. This condition is due largely to four causes: (1) early diagnosis; (2) better treatment (earlier and with arsphenamin); (3) prohibition, and (4) education.

Diagnosis is greatly facilitated by the state and municipal laboratories, in which the clinical findings or suspicions are verified by dark field examination and the Wassermann test. Arsphenamin is now within the reach of all. National prohibition will unquestionably diminish the number of primary lesions, and the free discussion of syphilis outside of medical meetings has caused many an old syphilitic patient to try to check up his physical condition by at least a Wassermann reaction, and many put themselves under treatment.

CLINICAL INSTRUCTION BASED ON PATIENT WITH SYPHILITIC LESIONS

The syphilitic patient with lesions is the real foundation of clinical instruction—not only for medical students and practitioners, dental students, and nurses; but also for the numerous agencies with their corps of workers who are turning to us for help and instruction, both medical and social; for syphilis, sooner or later, presents problems to all the agencies engaged in social betterment.

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

The growing practice of having a special department for the treatment of all stages and manifestations of both acquired and congenital syphilis has given the syphilographer a much wider scope of usefulness in the community. This condition is most gratifying. At the Massachusetts General Hospital we are in more or less intimate touch with about 160 different agencies or institutions, ranging from the municipal court with its probation officers, and the county jail, on the one hand, to the Bethesda Society (for the care of girls), the Children's Mission to Children, The Girls' Parole Department of the State, The State Department of Public Welfare, the Massachusetts Charitable Eye and Ear Infirmary, the Prenatal Clinic of the Boston Lying-in-Hospital, etc. Each has its own particular line of problems, but there is the same underlying cause as a meeting ground of common interest to us.

A society for the care of girls has recently arranged that all applicants for admission shall come to us for a complete physical examination, which includes a blood Wassermann test on all and a lumbar puncture when indicated. The two questions of gonorrhea and feeblemindedness are determined elsewhere. All the applicants have had some sexual experience. The advantages of a similar arrangement with the child-placing agencies is readily seen. It happens far too often that an apparently healthy baby with congenital syphilis is legally adopted, and the later syphilitic manifestations of eye, throat, or brain fall as a heavy burden on the foster parents.

The use of arsphenamin early in pregnancy has a pronounced effect on the viability and health of the fetus, so that many babies of syphilitic parents appear normal at birth. Such infants should be looked on as potentially syphilitic, and need most careful observation, or intelligent treatment, for an indefinite period. It is much harder to obtain the necessary co-operation from parents and attendants of these children when they show few or no signs of their congenital disease than when active lesions are present. It is also much more difficult to have precautions against infection carried out when there is no obvious reason for such a course.

Without the presence of infectious lesions it is difficult to teach the physicians and nurses in the public health courses. Syphilis then appears a benign infection. Practically the only lesions that are now available for demonstration are the ones new patients and occasional ward patients may show. The progress of repair in healing lesions may be of interest to the physician, but is of little teaching value. We all recall the days when especially typical cases were "booked up" for demonstrations several weeks in advance, without the least danger of treatment materially changing the character of the lesions.

The lack of material is especially felt in our work with the dental students, in whose instruction lesions in the mouth and throat, or about the face, are especially desired. One cannot assume the responsibility of the danger of contagion to associates by withholding arsphenamin from patients with infectious cases; and if arsphenamin is given, the desired patches are promptly healed. A recent house officer remarked that he had not seen over a dozen good examples of mucous lesions of the mouth during his two months' service in the department, with an average daily attendance of over a hundred patients.

It seems highly probable that the whole plan of teaching syphilids and the early infectious lesions may have to be changed, perhaps transferred from the out-patient to the wards, relying no more on ambulatory patients, but carrying out bedside instruction. Arrangements should be made for both teaching and isolation. Patients with infectious diseases that enter the ward now remain about ten days or two weeks, at which time they are returned to their homes with infectious lesions healed and only slight risk to their families. Their stay in the hospital has an educational value. These patients require less following up than patients that have not been in the ward. It is also easier for these patients to get leave from their employers to come for subsequent treatment.

At present there are about thirty beds available for infectious syphilitic patients in all the Boston hospitals combined, and throughout the state a large majority of the hospitals, both public and private, are still closed to syphilitic patients, either by custom, prejudice or the articles of incorporation. The infirmary of the state almshouse at Tewksbury has a considerable number of cases with demonstrable lesions most of the time, but the distance from the medical school is too great for its use as a teaching clinic under present conditions.

Several years ago surveys were made, in various clinics, to determine the number of hospital visits made by each patient with syphilis, and the results showed conclusively that most patients were simply treating symptoms, making no real attack on their disease. Of course relapses occurred. The introduction into the clinic of social service workers and a clinic secretary, with an adequate follow-up system, has already made a material improvement in these conditions. There are comparatively few patients now who do not receive at least one course of between six and eight arsphenamin injections, followed by a series of from twelve to fifteen gray oil injections, while many patients continue treatment until they are clinically and serologically cured. Under the present Massachusetts law, infectious syphilitic patients who lapse treatment for six weeks are reportable to the state board of health by name and residence. Then the state board notifies the local board, and the local board exerts the pressure necessary to bring the patient under treatment again. Through this means about 25 per cent. of these delinquents have been returned to the clinic.

From the therapeutic standpoint the vanishing lesion is most encouraging, but to those who feel that syphilis is still a disease that should be diagnosed by the clinical signs and checked up by the laboratory, rather than left entirely for its diagnosis to the serologist, the outlook is not reassuring. Thirty years ago we were told in our course on public health that, owing to the protective power of vaccination, probably none of us would ever see a case of small-pox. In general medicine today there is said to be insufficient material for the clinical teaching of typhoid fever; and I recently heard an internist say that steps should be taken to have a few cases of pulmonary tuberculosis once more cared for in the wards of the general hospital, that they might be used for teaching purposes.

PHYSICIANS RECOGNIZE SYPHILIS LESS READILY

With a decreasing opportunity for observing primary lesions and the early syphilids, the medical profession as a whole will become still less acute in recognizing syphilis, especially extragenital infections situated in unusual places and, as a result, small epidemics of (innocent) inoculations (like the one from kissing reported by Dr. Schamberg a few years ago) are likely to occur more frequently.

Within a year I have seen three cases in which the primary sore was excised by a competent surgeon for a supposed malignant growth (inside of cheek, lip and tongue). This is not said in criticism, but simply by way of emphasis. If competent surgeons are doing such things, how many more cases are being unrecognized by the members of our profession who, for one reason or another, are less well trained? There is a constant need of remembering to consider the possibility of syphilis in all "cold sores," lesions of tongue, tonsils or eyelids, which last over two weeks and thereby differ in character from the ordinary benign lesions. The hardness, painlessness, and accompanying enlarged glands, which appear early, should always suggest primary syphilis.

It is common knowledge that most of the primary lesions on the hands or fingers are found with those who care for the sick (physicians, nurses, dentists, etc.) ; yet, knowing this, what is so rare as the early diagnosis of a doctor's digital chancre? These cases are always maltreated by deep incisions, curetting and poulticings; and the diagnosis is often made only when a secondary eruption presents itself, or a positive blood Wassermann reaction is obtained. Often from three to six months have elapsed since the infection occurred, during which time the wife usually has contracted the disease. Men who have had good opportunities and should know primary syphilis failed to recognize these primary lesions. What can be expected of physicians of the future if we have not sufficient clinical material to give the proper instruction?

Extragenital primary lesions are apparently on the increase. The old conceded 10 per cent. seems now too small by at least 2 or 3 per cent. (If this increase is confined to Boston, I shall be glad to know it.)

Failure to recognize late syphilis may do some slight injury, but is not to be compared with such an oversight during the early stages. Syphilids often develop under cover of some other skin disease, such as scabies; and there have been several cases of extragenital infection of tongue, lip, tonsil, etc., associated with influenza in the recent epidemics, the primary lesions being ignored medically and the subsequent eruptions considered due in some way to the influenza infection. How many more cases of unsuspected syphilis have they created? Only eternal vigilance and the constant thought of the possibility of syphilis can prevent overlooking extragenital chancres. A routine histologic examination of all specimens from tonsillectomies, especially in adults, would detect certain cases of tonsillar chancre. A general physical examination, or even an inspection of the skin, would have shown the diagnosis and prevented needless operations in other cases of primary chancre of the tonsil.

The author has no desire to precipitate a quarrel with operators on the throat, laryngologists and others; but the fact remains that probably more chancres of the tonsils have been removed without recognition than all other extragenital primary chancres combined. Moreover, many of the patients were operated on with the secondary rash showing, and often the immediate object of the tonsillectomy was to relieve the acute painless swelling (the satellite bubo) of the tonsil gland. Little wonder then that we see physicians with primary lesions of the finger, contracted by performing a tonsillectomy in which the fingernail was used to free the tonsil from its capsule or in the removal of adenoid tissue. If it were possible to demonstrate primary syphilis of the tonsil to every medical student and carry home the conviction of the frequency of this condition, fewer tonsils would be removed before the possibility of syphilis had been considered and excluded.

During the war many civil conditions were temporarily given a military rating; and syphilis was once more brought into prominence as a venereal disease. With such a classification in the army and the navy, there can be no just criticism; but to class all marital, congenital and extragenital syphilis of civilians as a venereal disease is unfortunate and unfair. I trust there may be a concerted action on the part of the medical profession to overcome this renewed impression that syphilis and venereal disease are synonyms—in other words, that sin and syphilis are always inseparable.

During the past year an unusual number of undoubted early secondary syphilitic patients have been seen in whom the site of infection could not be determined in any way, there being absolutely no glandular enlargement or remains of a possible chancre. Is this to be the style of the future? Is the primary lesion also vanishing?

From a therapeutic point of view the outlook for the syphilitic was never more hopeful. Whether the present methods of treatment endure matters little, for they will be displaced by something better and perhaps be guided by more exact methods. The past decade and a half has seen the application of practically all our present methods of precision: dark field, roentgen ray, animal inoculation, cultivation of spirochetes, spinal and ventricular punctures and study of these fluids, together with the Wassermann reaction. These tests also will stand until replaced by something better.

The widespread use of arsphenamin is chiefly responsible for the scarcity of lesions. With a prompt recognition of primary syphilis and more general use of arsphenamin, subsequent lesions will be still more rare. This applies not only to skin and mucous lesions, but to those conditions occurring years after infection, some of which have quite recently been shown to be almost exclusively of syphilitic origin—aneurysm of the aorta and aortitis. We now believe that the foundation for these lesions, like the foundation for tabes and paresis, is laid during the early secondary stage of the disease. The same condition undoubtedly holds true for most of the visceral lesions and probably for many of the late skin outbreaks as well. Adequate treatment, given in the primary or early secondary stage, should practically eliminate all the subsequent lesions, thereby working a radical change in all fields of general and special medicine.

TEACHING SUBSTITUTES FOR SYPHILITIC LESIONS

What are the teaching succedanea for syphilitic lesions? Ordinary photographs are but poor helps, showing only the site, number and relative size of lesions that lose much of the instructive value by their lack of correct coloring. Few of the atlases of colored plates are of practical value. Water color paintings of skin lesions are expensive. Wax models are expensive, and impracticable for use in class exercises or with large sections. Our greatest hope would seem to be in the application of color photography. If this can become available, some of the threatened dangers will be overcome as far as the recognition of signs by sight are concerned. Nothing can ever supplant the knowledge of indurations to be gained by handling. Touch and appearances must be appreciated together.

To supply these teaching outfits seems a fitting undertaking for some of the philanthropists or foundations interested in the question of better teaching in our medical schools. Can a better use be found for some of the money available for improving teaching conditions in our medical schools than in producing and perfecting sets of colored negatives and wax models that can be utilized in teaching primary lesions, the skin eruptions or mucous lesions of syphilis? By preparing colored negatives or lantern slides in a central plant or factory, sets or collections could be supplied at a much lower cost than would be the case were each school to make its own, and the collection would be more nearly complete.

There is hardly another field in medicine in which failure to make a correct diagnosis carries such grave consequences, not only to the patient, but to the family and to the community. Failure to use prophylaxis against ophthalmia neonatorum is a punishable offense in Massachusetts, as is the failure to report such condition to the board of health, when it exists. Prosecutions have occurred. The injury to such a baby may indeed be great, but the failure to recognize that a baby has congenital syphilis often means the early death of the child, though not infrequently the child lives long enough to infect some of its attendants or family. Many of the primary lesions occurring about the face in adults are the result of fondling an unrecognized syphilitic baby. Only recently has syphilis been added to the list of reportable diseases in Massachusetts.

SUMMARY

It seems probable that secondary and tertiary lesions of syphilis will continue to occur less and less frequently. This serious problem in teaching must be anticipated and solved by:

1. Provision of sufficient beds to care for the acutely infectious cases that cannot be properly isolated at home.
2. The segregation of syphilitic patients into one department, in which the various phases of the disease can be studied and treated.
3. Collecting photographs of all lesions that can be shown by prints or lantern slides.
4. Applying (if possible) the color process of photography.
5. Wax models—moulages—utilized to a greater extent in European medical schools and hospitals than in America. A plea for their production and use here was made by Dr. Wallis at the last meeting of the American Medical Association. These models will always be expensive and therefore not freely available.

DISCUSSION

Dr. Wile said that those who were engaged in teaching syphilis must be distinctly interested in Dr. Smith's paper. His experience had been the opposite of Dr. Smith's and the amount of material they were seeing today was much greater than that they were seeing many years ago; he believed this was due to the fact that syphilis was being centralized in their department, where previously it was not. Dr. Wile believed that the Utopia of the elimination of syphilis—so desirable, of course, from the patient's standpoint and undesirable from the teaching standpoint—was yet far off.

In regard to syphilis, Dr. Wile felt that the material was just beginning to be properly used for the purpose of instruction.

If the condition described by Dr. Smith should become general, Dr. Wile felt that any other substitute for the human subject, whether it be the actual photograph or the colored photograph, would fall far short of satisfaction. He believed that the living subject, not only in syphilis but in any other disease, was the only practical and desirable way of teaching the clinical aspects of the disease, as far as undergraduate students were concerned.

Dr. Wende stated that from observations in Buffalo he could substantiate those of Dr. Smith of Boston. He found, as did Dr. Smith, that material for the practical clinical teaching of the skin manifestation of syphilis is growing less and less owing, in his opinion, to the widespread early use of arsphenamin. He believed that he is now seeing but one case of typical skin lesions to five formerly. During the last two or three years in his classes in the dental school he had been unable to demonstrate satisfactorily syphilitic mucous membrane mouth lesions because of the scarcity of their appearance in his clinic.

In regard to the technic in securing photographic reproductions, he felt that today the ordinary black and white photography gave the best results obtainable. He had made many attempts to use color photography since its inception, but found the results not so satisfactory. He had also for several years had photographs colored by competent artists but had always found that in applying the colors much of the important and essential detail was erased or at least befogged, especially in lantern slides. In order to secure detail in high relief he had always found flashlight very unsatisfactory, but long exposure in good natural light with small lens aperture had always given him the most satisfactory results. He stated that all his reproductions were so produced; however, he appreciated the great excellence of the reproductions exhibited by Drs. Fordyce and MacKee.

Dr. Irvine agreed with Dr. Smith in regard to the vanishing lesion of syphilis. He thought they saw about the same number of active lesions (but not the same percentage), but that was because of the increase in their material. It was not infrequent in a clinic of fifty to seventy-five patients a day to have not a single skin lesion from which to teach. He thought Dr. Smith's paper was timely and, as brought out by Dr. Stokes in his paper, one must teach all the manifestations of syphilis and not center on the cutaneous ones alone. As time goes on it will become more and more necessary to teach syphilis from all standpoints.

Dr. Grindon agreed with Dr. Wende regarding the superiority of black and white over other pictures for those who were already familiar with the lesion and the disease. These would unconsciously add the color element and picture to themselves the lesions. On the other hand, to the man who does not know the lesion and has to be taught, it does not carry a full and true impression, no matter how close a reader he may be. It was a fact that no reproduction, whether it be by color photography, moulages or anything else, can take the place of the lesion on the living subject. Palpation was just as important as the use of the eye, but perhaps in the future one will have to choose from imperfect methods.

As to the actual condition confronting the profession at present, Dr. Grindon's teaching is done with material at the St. Louis City Hospital. While clinical material is diminishng, there is still enough for teaching purposes. However, he feared that the time was not far distant when they would experience a similar condition to the one now existing in Boston. Probably early treatment was not as systematically employed in St. Louis as in Boston. There might be a way out of the difficulty as it existed in St. Louis and other large centers, furnished by the out-clinics conducted by private charities or associations where the early treatment of syphilis is carried out, ofttimes in the evenings. So far as he knew, this material in his city had not been utilized. It might be a wise plan to transfer the greater part of the teaching of early syphilis to out-patient departments in which patients came with primary and early secondary lesions.

Dr. Howard Fox thought that too much emphasis had generally been placed on the value of colored photographs in portraying skin diseases. While high class colored photographs were, of course, of great value for teaching, the element of color was often of distinctly less value than the distribution, configuration and character of the lesions. Dr. Fox had recently been experimenting with a comparatively new method of illumination for photography, an electric lamp of 1,000 watts, with blue lamp and reflector. It was especially suitable for physicians having a small space available for photographic work and was a quick, clean and convenient method. It was best suited for localized areas of the body. One objection was the difficulty in avoiding a dark shadow on the background, as the rays of light were concentrated in contradistinction to the diffused character of daylight and flashlight.

Dr. McEwen thought Dr. Smith's paper was timely. In Chicago the material showing syphilitic lesions was greatly reduced, mouth lesions especially were becoming far less common. The mucous patch is seen today with nothing like former frequency.

He thought the percentage of extragenital chancres generally accepted was far too low and believed there should be a greater emphasis on the possibility of extragenital chancres in the consideration of syphilis.

He considered the solution of the problem raised by Dr. Smith to be in the use of models, and he would like to see moulages of skin diseases much more extensively used in teaching, not only the lesions of syphilis but also the primary and consecutive lesions of the skin with which the beginning student of dermatology must struggle.

Dr. Engmann thought one point should be emphasized in regard to the disappearing lesion. Certainly all had noticed that it was difficult to obtain proper material for teaching. It had occurred to him that a different strain of syphilis might be developing. It was a question whether this was due to the arsphenamin alone, or whether it had affected the chemical affinity of the spirochete. Every one knew that there was an enormously increased percentage of visceral and nerve syphilis, and while this might be due to a large extent to the improved methods of diagnosis, it had occurred to him that there might be a change in the chemical affinities of the organism.

Dr. Stokes believed it was possible to reconcile the views of Dr. Smith and Dr. Wile. The available material in acute and early syphilis depended on the source from which the clinic was drawing. When he went to Rochester he saw practically no early syphilis; all the syphilis was late and of an unfavorable type for treatment. But of late he had seen more and more cases of early syphilis because many patients were becoming critical of the general practitioner's antiquated methods and traveled to the place where they had heard syphilis was being treated properly. This is a phase in the development of every clinic; the long-standing clinics which have been doing their teaching work among the profession effectively, eliminate the work that is coming to them. On the other hand, the newly established clinic that is doing good work draws early cases to it until its methods become common property. Both clinics are effective in different phases of the disease.

Dr. Stokes had tried experiments in giving photographic clinics. This was the only method available to him at first in teaching the large body of Fellows at the Mayo Clinic. He had become firmly convinced that it was not color which made the diagnosis of the lesion. If color photography sacrificed detail it should not be used, for it was the detail that did the teaching work. In looking at Dr. Wende's beautiful pictures he was at once impressed with their detail. He had tried the experiment of getting as much detail as possible in a photograph and then enlarging it. A man could be taught in this way to diagnose erythematous lupus, for example, from the photograph. When a case was later encountered in the clinic, he could at once pick it up.

Dr. Stokes believed Dr. Smith was right, that there would be progressively fewer visible lesions, and that students should be taught diagnosis by objective signs that do not depend on the mere visibility. They should acquire all of this knowledge possible against the day when there will be little early syphilis to see and teach from, but perhaps a great deal of late syphilis to cope with.

Dr. Schamberg could not bring himself to the belief that there had been any increase in visceral syphilis through the introduction of the newer methods of treatment of this disease. He thought there was an apparent increase, due to a more enthusiastic and careful search for these lesions.

Dr. Smith (closing) agreed with Dr. Schamberg that there was no increase in the number of visceral cases, except that they were checked up and recognized by the newer methods of diagnosis. The number of patients in his clinic was constantly increasing. The department was started in 1914 with thirty-five patients and now there was a maximum attendance of 160. Many of the patients have received one, two or three injections of arsphenamin outside, and then have heard, possibly, that they were not receiving just the line of treatment they should receive and come to the clinic. If these patients are examined they usually show serologic evidence and perhaps a certain amount of clinical evidence that they are syphilitics, and while they make up a large bulk of the work, they are practically worthless for teaching purposes.

Dr. Smith agreed with Dr. Grindon, who said that one unconsciously pictured to himself the proper color in the black and white photograph, which is practically impossible for the student who has no standard of color for the various skin eruptions. He considered the colored photographs of great assistance and hoped that through some sort of process it might be possible to reproduce colored prints that would be of more value than the ordinary black and white.

STREPTODERMATITIS, ESPECIALLY IN ITS RELATIONSHIP TO WOUNDS

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Streptodermatitis as a complication of wounds may give rise to a degree of misery and discomfort far surpassing its evident seriousness. The best general description of this form of dermatitis is that it resembles a superficial burn. The bright red patch may spread by a sharp margin, and so remind one of erysipelas, from which it differs in its superficiality. In other cases it may spread by dissecting along under the horny layer of the epidermis, causing a ragged undetermined border, or it may extend by minute, diffusely scattered red spots, which gradually coalesce with the main patch. The surface may be red and raw and may weep a clear serum like a recent burn; or it may be purulent and covered with crusts; or it may be finely vesicular or bullous, resembling a vesicular eczema. The latter phase may occur in eczematous patients, and is often designated acute vesicular eczema. In any form the itching and burning may be tormenting and may constitute a most serious embarrassment to the patient recovering from a wound:

The features of the disease demanding special consideration during treatment are:

First, streptodermatitis is an infective disease, and therefore requires the employment of antiseptics. Second, the septic agent, a streptococcus, is an anaerobe and therefore many forms of occlusive dressing are inadvisable as favoring its growth. Third, the skin is in a highly irritable condition, and all topical applications, which are at the same time irritating, must be prohibited. In fact, the antiseptics employed should be, as a rule, so dilute as to be nonirritating to the skin, and should be inhibitory rather than annihilating to the microorganisms.

SOLUTION OF LEAD SUBACETATE

For a long time dermatologists and surgeons employed this agent on wounds and on raw infected surfaces, supposing that it controlled inflammation by its styptic or astringent action on the tissues and blood vessels. The principle of oligodynamic action, first enunciated in a posthumous paper by Naegeli in 1893, may afford an explanation.

OLIGODYNAMIC ACTION

The epithet oligodynamic[1] is given to the poisonous action of minute traces of certain metals in water, such as copper or lead. The metals in question are present either as the hydroxid or carbonate in the colloidal state. Historically, it is highly interesting that it is these two metals, the acetate of lead as Goulard's extract and the sulphate of copper, or eau d'Alibour, which have been used for so long, and in a very dilute solution, as tropical remedial agents for external inflammatory conditions. We shall consider the probable mode of action of lead.

Acetate of lead in the presence of a fluid, such as serum rich in carbon dioxid, would form carbonate of lead, a particularly bland form of this bland and unctious metal. This change of the acetate into the carbonate is so inevitable and so easy that it constitutes the commercial way of making white lead. In this process, lead buckles are placed in jars of vinegar, thus forming the acetate, and these jars are exposed to the carbon dioxid gas emanating from the fermentation of tan bark. At ordinary temperatures the carbon dioxid is the stronger radical and displaces the acetate, thus forming the carbonate. Similarly, the acetate of lead in a lotion would turn into the carbonate by coming into contact with the carbon dioxid in a serum oozing from a pathologic lesion. Furthermore, the carbonate would precipitate in very fine division and in a medium admirably adapted to its becoming colloidal.

Copper seems to be the most powerful of these oligodynamic metals. Naegeli estimated the amount of copper present in 12 liters of distilled water, which had been four days in contact with twelve two-pfennig pieces, as being one part in seventy-seven million, yet it was powerfully toxic to Spirogyra, killing it in one minute. Copper lotion as eau d'Alibour has always been a favorite in France, but has never become so either in England, Germany or America. On the other hand, lead lotion, in spite of profound changes in surgical technic, has never been displaced entirely in any of the latter countries.

Solution of lead subacetate consists of lead acetate 180, lead oxid 110 and distilled water to make 1,000. A mistake frequently made is to employ it too strong. A teaspoonful to a pint of distilled water is quite strong enough; we usually use it in one fifth of this strength. So diluted and employed soaked in a compress, and covered with oil silk or rubber tissue, it does not interfere with the penetration of the water into the epithelial tissues, nor with the natural exfoliative processes of the epidermis, which are such a great aid in carrying off superficial bacterial invaders.

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[1] Bayliss, William M.: Principles of General Physiology, 1915, pp. 108 and 222.

If itching is a feature, and it often is, a coal tar can be added to the lead. Hutchinson's lotion acts admirably in such a case:

℞ Solution of lead subacetate...................... ℥ss
Solution of carbon detergent.................... ʒiiss
Sig.: Hutchinson's lotion. A teaspoonful in a pint of warm water to use as a lotion.

This may be further diluted by employing two pints of water instead of one. The fact that the lead water, added to the tar liquor, is an incompatible mixture, forming a dirty greenish gray precipitate, does not appear to interfere with its efficacy. Such a mixture may be applied for hours with the greatest benefit.

A boric acid solution, made by adding one or two tablespoonfuls of boric acid powder to a gallon of hot water, also makes an admirable lotion. The boric acid acts as a mild antiseptic and also renders the water bland and isotonic. The addition of 10 per cent. of liquor alumini acetici to this is excellent. Aluminum acetate is a mild and efficient antiseptic, and it acts better in a dilute solution than in a strong one.

Silver, as well as lead and copper, has also an oligodynamic action, and has long enjoyed a reputation in this kind of dermatitis. Gougerot[2] advises its use in a 10 per cent. solution, applied once or twice a week. I think a better effect is obtained from the use of a much more dilute solution applied for a longer time, though not necessarily at shorter intervals.

Nitrate of silver solution is excellent for injection into fistulas and suppurating cavities, which may act as the focal origin of the dermatitis.

When it is desired to change a wet dressing for something else because of its being damp and soggy, a drying lotion containing a great deal of powder, or a paste containing a great deal of powder mixed with a fat such as petrolatum may be prescribed. An ointment should not be employed because it is too occlusive. The powdery lotions referred to above and pastes soak up the discharges instead of damming them back as an ointment would, and they allow the escape of heat, and do not absolutely preclude the air, an important point when dealing with anaerobic bacteria. An indifferent powder such as starch, zinc oxid, or talcum or a combination of them may be used with the addition of 1 to 2 per cent. of salicylic acid. Care should be used in employing boric acid, as even when finely powdered, there are broken crystals in it which irritate the tender skin like particles of glass. In solutions these crystals are destroyed, and when boric acid is incorporated, whether in a paste or in an ointment, care should be taken, for the same reason, to melt it first, either with glycerin or fat.

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[2] Gougerot, H.: La Dermatologia en Clientele, 1917, p. 398.

Very often the crusting is a serious matter in this form of dermatitis. The formation of crusts may be regarded as a defensive measure on the part of the micro-organisms, as being anaerobic they pullulate better on the exclusion of air. It is necessary to remove the crusts without undue violence. A preliminary soaking with the above mentioned lead or boric acid lotions often answers well.

A boric acid starch poultice is often excellent for removing the crusts and for relieving congestion. It is made by adding a heaping tablespoonful of finely powdered common laundry starch to two tablespoonfuls of cold water, and then adding to this a coffee cup full of boiling water, stirring rapidly until the mixture forms a thick paste. To this paste should be added a tablespoonful of boric acid powder, stirring until it is dissolved. Starches differ a little in their paste-forming quantities, some requiring a little more and some a little less of the starch powder to form a paste of the proper consistency for a poultice.

CLEANING THE SURFACE

Cleaning the surface of the highly irritable skin from its débris of cells, fat, pathologic secretions, crusts and dried on, precipitated applications is an important matter. Plain water is even more unsuitable than on the normal skin, as the oily surface sheds it and it is hypotonic. The addition of soap, as in our daily ablutions, makes the water still more irritating. The addition of boric acid improves it, but it is not sufficiently detergent. Alcohol, so admirable in many situations, is too sharp. Benzin or gasoline is excellent, as they are wonderfully solvent for both fats and crusts and rarely irritate.

Under a well directed treatment, streptodermatitis disappears in from six to eight weeks or sooner, except when complicated by eczema, when the duration of the malady may extend into years.

The important matters to remember are that this dermatitis is an infective disease demanding the employment of antiseptics which must be mild and must be used very dilute. Occlusive dressings are not to be employed. Moist dressings, as indicated, and pastes, in which the amount of powder in the fatty base is great (50:50), are not occlusive in the sense meant. In cleaning the affected surfaces, only mild measures are permissible.

Streptodermatitis may arise from a chafing or from a slight abrasion which, by the time the disease is in full swing, has disappeared. Sometimes, however, its seat of origin is clearly in evidence, as in a suppurating wound or at the mouth of a fistula leading, for example, from an osteomyelitis. It may arise long after the wound—the site of its origin—has healed, as in a case which came under our observation a short time ago. The original patch having started, it may be transferred by the hands, especially by the nails, to different parts of the cutaneous surface. It may spread over the entire cutaneous surface, including the face, scalp, palms, and soles, and so give rise to a kind of dermatitis exfoliativa. The misery of the patient can then be said to be complete.

News and Comment

SPIROCIDE (MERCUPRESSON)

Several physicians have written to the Archives of Dermatology and Syphilology concerning a circular that they have received extolling the virtues of "spirocide (mercupresson)," in the treatment of syphilis. Accompanying the commercial circular is a reprint by Dr. J. Lewengood reporting the results, surprising to him, which he has obtained in certain cases of syphilis by using this remedy. On examination it proves to be a combination for administering fumigations. In addition to mercury, it contains certain vegetable substances and copper. The use of vegetable substances—"alteratives"—for the efficient treatment of syphilis belongs to past days. In this preparation they are burned up anyway. If the copper were volatilized at all, it would be of no known virtue in syphilis. The treatment, therefore, reduces itself to a method of mercurial fumigation. The treatment of syphilis by fumigation can, of course, be used effectively. It was used in the dawn of the history of syphilis, but it has not maintained its position, chiefly, doubtless, because it is inexact and dangerous. As a new means of treating syphilis spirocide is about in the class that the sixteenth century blunderbuss is among firearms. Neither the commercial claims nor the so-called scientific claims which it furnishes are entitled to serious consideration.

It is depressing that efforts to exploit us with things of this sort are constantly recurring, and it is deplorable that endorsements of such remedies are given on the basis of uncontrolled experiments by captains, majors, colonels, state public health officials and other medical men who should be careful of what they endorse. Experience is fallacious, and judgment difficult, particularly with remedies for syphilis.

THE DEATH OF DR. ISADORE DYER

Dr. Isadore Dyer, dean, and professor of diseases of the skin, Tulane University of Louisiana School of Medicine, New Orleans, died on October 12, 1920. An obituary will appear next month.

Abstracts from Current Literature

RELATION PATHOGENIQUE ENTRE LES LEUCEMIES ET CERTAINES DERMOPATHIES (THE PATHOGENIC RELATION BETWEEN THE LEUKEMIAS AND CERTAIN DERMATOSES).

L. M. Bétancès, Haematologica **1**:1 (April) 1920.

Mr. Bétancès has written a very interesting and complete monograph on the subject of the etiology and pathogenesis of the cutaneous manifestations of leukemia. In the first place he believes that the theories concerning the hemopoietic organs and their function are erroneous. After numerous histologic examinations of the lymphatic glands and spleen and of the cutaneous lesions in cases of leukemia, he has been able to prove that all the symptomatic complexes known under such names as dermatitis exfoliativa (Wilson-Brocq), pityriasis rubra (Hebra), dermatitis polymorpha (Brocq), dermatitis premycotica, lymphosarcomatosis (Sternberg), chloroma, myelomatosis (Kahler), adenia (Trousseau), Hodgkin's disease, mycosis fungoides, lymphadermia (Kaposi), lymphogranulomatosis (Paltauf-Sternberg), leukanemia and leukosarcomatosis are due to disturbances of hemopoiesis. According to him, Ehrlich's hemopoietic dualism is a false conception. He thinks that instead of two different hemopoietic tissues, that of the marrow of the bones and that of the lymphatic glands and the spleen, producing respectively, the myeloid and the lymphoid cells, there is only one which may produce, as required, myeloid or lymphoid cells. This hemopoietic tissue is situated in the bone marrow, the lymphatic glands, the spleen, and also in a latent state in the connective tissue of the body. He quotes: "The specific hemopoietic tissue (hemocytoblastic) and the diffuse hemopoietic tissue (hemohistoblastic) are embryologically and physiologically identical; thus they form a single anatomic system which may be termed the hemopoietic parenchyma or unity." (Ferrata and Negreiros, Rinaldi, A. Ferrata.)

After a short review of the pathogenesis of the leukemias, which he considers a hyperplasia of the hemopoietic parenchyma, Bétancès refers to the histologic changes in the lymphatic glands, bone marrow, spleen, liver, kidneys, tonsils, lymphoid nodules of the intestines, blood vessels and skin. The cutaneous lesions may be generalized or localized. The skin is thick, swollen, sometimes red and oozing and sometimes reddish yellow or gray and dry. The epidermis is covered with scales of variable size, rather thin and dry; the hair and nails show dystrophic changes and may disappear entirely. Occasionally the erythroderma remains localized and there is the formation of bullous lesions, psoriatic plaques or eczema (polymorphous erythema). Sometimes there are nodules and tumors, which may ulcerate. Microscopically there are, in the papillary region and in the corium, numerous lymphoid cells, hemocytoblasts, lymphoblasts and Ferrata's monoblasts. The connective tissue forms a sort of wide meshed reticulum filled with these cells, which occasionally form masses around the blood vessels. Mast cells and plasma cells, eosinophils, neutrophils, and some peculiar blood cells like those described by Turk and Rieder are abundant in certain cases. The changes in the epidermis are those of atrophy and dyskeratosis.

The author's conclusions are:

1. Dermatitis exfoliativa (Wilson-Brocq), pityriasis rubra (Hebra), dermatitis exfoliativa (Vidal-Leloir), polymorphous dermatitis (Brocq), dermatitis premycotica, lymphosarcomatosis (Sternberg), chloroma, myelomatosis (Kahler), adenia (Trousseau), Hodgkin's disease, mycosis fungoides, lymphadermia (Kaposi), lymphogranulomatosis (Paltauf-Sternberg), leukanemia, leukosarcomatosis and all other forms of leukemia, are diseases of the hematopoietic system.

2. The pathogenic process in all these diseases is exactly the same. It consists of a hyperplasia of the hemopoietic histologic unity, with a total or partial incapacity of the same to form differentiated myeloid or lymphoid cells.

3. This process is caused by certain lymphotoxins, myelotoxins or toxic lipoids acting on the hemopoietic unity and producing an exacerbation of its function.

Pardo-Castello, Havana.

EXPERIMENTAL PELLAGRA IN WHITE MALE CONVICTS. Joseph Goldenberger and G. A. Wheeler, Arch. Int. Med. **25**:45 (May) 1920.

This work was carried out at the Rankin farm of the Mississippi penitentiary on eleven convicts who volunteered for the test. Those chosen had no previous history of pellagra either in themselves or in their families. The volunteers were placed on shorter work hours and had regular rest periods, their work being in the fields and classed as moderate or light.

The observations extended from February to October. There was no change in food until April 19, but the diet was restricted after that date. The average intake of each patient varied from 2,500 to 3,500 calories, 41 to 54 gm. of protein, 91 to 134 gm. of fat and 387 to 513 gm. of carbohydrate. The diet consisted of highly milled wheat flour, maize meal and grits, cornstarch, white rice, cane sugar, cane syrup, sweet potatoes, pork fat, cabbage, collards, turnips, turnip greens, coffee, "Royal" baking powder, salt and pepper.

None of the control patients developed pellagra, although in contact with it, while six of the eleven experimental patients developed evidence of this disease, the first symptoms appearing during the second month of the test diet. These symptoms were weakness, abdominal discomfort and headache; loss of weight became marked in the last few weeks of the experiment.

Six of the eleven developed skin lesions, beginning about five months after the institution of the diet, the first lesions beginning on the scrotum; later lesions appeared on the hands in one case and on the neck in another.

The authors consider that these six patients developed pellagra as a result of the experimental diet and they emphasize the early development of the scrotal lesion which appears to be much more common as an early symptom than has been previously recognized. They state that there may be certain qualities in diets which determine the initial dermatitis of an attack, these differences in quality corresponding to certain differences in clinical types.

They further state that the "dietary factors to be considered as possibly essential are (1) amino-acid deficiency, (2) faulty mineral supply, and perhaps (3) an as yet unknown (vitamin) factor."

Jamieson, Detroit.

DIE ENTWICKLUNG UND DER HEUTIGE STAND DER ROENTGENBEHANDLUNG DES FRAUENBARTES (THE DEVELOPMENT AND PRESENT STATUS OF ROENTGENOTHERAPY OF FACIAL HYPERTRICHOSIS IN WOMEN). Fritz M. Meyer, Dermat. Ztschr. **29**:334 (June) 1920.

The history of the roentgen-ray treatment of hypertrichosis is given, with an outline of the writer's experiments in this field. The present method is to divide the face into six or eight parts, when one is dealing with a universal hyperthricosis, and to ray each area for three "Volldosen" (510 F., according to Fürstenau) through 4 mm. of aluminum. After fourteen days the hairs begin to fall out, and after twenty-five days the epilation is usually complete. It is necessary, six weeks after the first radiation, to repeat the treatment, and a third application of an equal dose is given eight weeks after the second. The three sessions are necessary for success in favorable cases (those in which all the hair falls out after the second exposure). In general, one or two more rayings are given, at ten week intervals after the third. These later exposures may be one-sixth smaller than the early ones. Black, long hairs are most favorably influenced; long thin down is less favorable, and light small down growths are very refractory. The hairs of the upper lip fall with difficulty and return easily. In otherwise successful cases, the upper lip may have to be given individual raying.

The skin and mucous surfaces of the face are swollen after the exposures, and there is a drying of the mouth, with loss of salivary flow and diminished appetite. If the exposures are repeated too rapidly, headache, neuralgia, indisposition and lassitude may follow and persist for from twenty-four to forty-eight hours. The gums are protected by rubber infiltrated with lead, and pains which were frequent before this refinement of technic was introduced have not been complained of since. No permanent injury has been done.

Goodman, New York.

LA PONCTION LOMBAIRE DANS L'INTOXICATION PAR L'OXYDE DE CARBONE (LUMBAR PUNCTURE IN CARBON MONOXID POISONING). Legry and J. Lermoyez, Bull. de l'Acad. de méd. **84**: 67 (July 27) 1920.

In carbon monoxid poisoning the reaction must be thought of more as a corticopial congestive and hemorrhagic process which the intoxication produces than as an intoxication. In a recent case, the writers on their first lumbar puncture found a spinal fluid which appeared like almost pure blood. Such evidence of a hemorrhagic state is not constant in all cases. Lesieur and Rebattu have reported cases with spinal fluid free of all anomaly. Though the patient whose case is cited showed a bloody spinal fluid and serious symptoms, his wife and daughter presented only transitory malaise though subjected to precisely the same exposure to the gas. To explain this peculiarity, the authors mention the writings of Balthazard and Nicloux and of Bollet. While in normal persons the coefficient of intoxication is very constant, it is noticeably lowered in the person with a coexisting defect, such as chronic nephritis or hepatic cirrhosis. Other similar visceral alterations can assuredly lower resistance. Regarding their own case, they conclude that the patient's point of weakness lay in the nervous system itself. In the war he had had cerebrospinal meningitis and twice had suffered concussion with loss of consciousness. Such antecedent occurrences are enough to create a special vulnerability to the gas in spite of the small amount inhaled.

It is suggested that chemical examination of the spinal fluid offers a means of diagnosis in uncertain cases.

Davis, New York.

KLINISCHE UND HISTOLOGISCHE BEOBACHTUNGEN AN TAETOWIERTEN (CLINICAL AND HISTOLOGIC OBSERVATIONS OF TATTOO MARKS). E. Arning, Arch. f. Dermat. u. Syph. **123**:225, 1916.

Tattooing is universal among sailors. Only the South Sea Islanders mark the face. The most beautiful work is done by the Japanese. Prostitutes and criminals also have much tattoo. The Japanese use India ink for blue-gray, cinnabar for red, indigo and curcuma for green, and curcuma alone for yellow. European tattoo workers use India ink, carbon, cinnabar and occasionally carmin. Arning had the opportunity of studying several cases in which the use of cinnabar for tattooing resulted in a local reaction which clinically closely simulated tuberculosis verrucosa cutis, and indeed several dermatologists made that diagnosis, considering that the organism of Koch was introduced with the sputum used to mix the tints. It was easily disproved, however, because only the red gave the reaction, and all of the tints were mixed with the same sputum. Arning considered that he had to deal with an idiosyncrasy to mercury, which he demonstrated by applying a square of mercurial plaster to the patient's arm, with a resulting local reaction. He pictures a moulage of cinnabar dermatitis and the reaction to mercury plaster.

Arning also observed a patient with secondary syphilis, in whom the red areas of his tattoo (mercury sulfid) were free of lesions. Dohi first called attention to this relative immunity in 1909, since which time Florange, Holland and others have reported cases. Arning does not believe it is the result of any spirocheticidal effects of the mercury salt deposited in the skin, but of the local infiltration reaction to the foreign body. He is still working on this phase of the problem.

Goodman, New York.

EPITHELIOMATOUS ULCERATION AMONG TAR WORKERS. W. J. O'Donovan, Brit. J. Dermat. **32**:215 (July) 1920.

O'Donovan states that the increasing importance which is being attached to the industrial etiology of disease is reflected in the increasing number of occupational diseases that are being made notifiable. Epitheliomatous ulceration due to tar, pitch, bitumen, mineral oil or paraffin, or any compound, product or residue of any of these substances, and chrome ulceration are the latest diseases made reportable.

The author cites the widespread and increasing use of these substances in present day industry, and gives figures showing the frequency of occurrence of warts and epitheliomas among workers. A review of the literature shows that Volkmann in 1875 was probably the first to call attention to a definite industrial tar etiology of malignant disease.

In considering the clinical aspects of the subject O'Donovan cites a number of cases, and finds the following outstanding points in regard to tar epitheliomas:

(1) There is a variation in age among those affected with carcinomatous lesions.

(2) Long duration of employment is common before the development of serious lesions.

(3) Many growths that have needed operative treatment have a short history.

(4) In a few cases single lesions of long duration have needed operative relief in the end.

(5) Although tar warts may have existed for years, even twenty-five, the change in type and rapid growth of a new lesion causes the worker to seek early surgical advice.

The prognosis in these cases is good, and papillomas, in all respects similar to other tumors removed and proved microscopically to be carcinomatous, have generally fallen away after from two to four months duration. Treatment is surgical, though there is no objection in the case of new lesions to deferring operation for a few months to see if a natural cure is probable by dehiscence.

Senear, Chicago.

TUMORS OF THE BLADDER, INCLUDING REPORT OF VEGETATING SYPHILOMA OF THE BLADDER. W. C. Danforth and B. C. Corbus, Surg., Gynec. & Obst. **31**:219 (Sept.) 1920.

During seven months, seven cases of bladder tumors have been observed. One patient presented condyloma which closely simulated a true tumor growth. This woman was 25. She complained of pain over the lower abdomen, painful and frequent urination, and loss of weight. A Wassermann test, made three days after admission, was slightly positive; a second test two days later was negative. Cystoscopy showed the entire bladder floor occupied by an infiltrating growth with many peaked projections of papillomatous character, together with larger, rounded masses, the upper portions of which showed a translucency indicating edema. A small piece of tissue was secured by cystotomy and examined. The pathologist reported that, while the specimen had been somewhat injured by drying, none of the sections showed malignancy but merely appeared to be necrotic material. The patient was given nine intravenous arsphenamin injections. She immediately began to improve and cystoscopy disclosed a marked regression of the growth at the base of the bladder, the distinguishing characteristics of which, however, were still plainly visible.

(Dr. Leo L. Michel has called my attention to two plates in "Traité pratique de cystoscopie" by Marion, Heitz-Boyer and Germain [Masson et Cie, 1914], entitled "Bullous edema on lateral face of bladder," and "Bullous edema of a particular form situated on the upper part of bladder," which closely resemble the figures pictured in the article of Danforth and Corbus.)

Goodman, New York.

UEBER DEN VERLAUF DER AUF DEN MENSCHEN UEBERTRAGENEN TIERSYPHILIS (PROGRESS OF HUMAN SYPHILIS ACQUIRED THROUGH ANIMALS). A. Buschke, Arch. f. Dermat. u. Syph. **123**:278, 1916.

Buschke reported in 1913 the case of a laboratory assistant who acquired syphilis from a rabbit. The subsequent history of this patient is presented. Buschke is led to believe that the virus was not reduced in virulence for man by passage through at least six or seven rabbits. There are two other incidences in the literature of syphilis transferred back to man from rabbits. In neither case is there reason to believe that the disease ran a milder course than human to human infection. In one of these cases, there had been sixteen rabbit passages of the infectious material. Metchnikoff reported two cases of syphilis transferred back to humans from apes. In both these the disease is supposed to have run an exceedingly mild course.

Goodman, New York.

UEBER QUECKSILBERINJEKTIONEN BEI KINDERN UND SAEUGLINGEN (MERCURY INJECTIONS IN CHILDREN AND INFANTS). Johan Almkvist, Arch. f. Derm. u. Syph. **121**:895, 1916.

Mercury may be given to nurslings and young children with good clinical results in syphilis. Children under 1 year, for example, may receive 2 mg. per kilo of weight every third day for a course of ten injections. Increase in weight is a guide to the condition of the patient.

Goodman, New York.

INDUSTRIAL DERMATOSES, THEIR SOURCES, TYPES AND CONTROL. W. A. Pusey, Proc. National Safety Council, 1919, p. 632.

In this paper, read before the health section of the National Safety Council, Pusey reviews in a general way the subject of industrial dermatoses, discussing the rôle played in their production by (1) heat, (2) cold, (3) weather, (4) posture, friction, pressure, (5) parasites, (6) infections, and (7) mechanical and chemical irritants. He calls attention to the extent and importance of the problem of industrial dermatoses, neglected because the experts in industrial medicine are not trained in dermatology, and recommends that one way of undertaking systematic investigation would be to employ a few trained dermatologists to devote all their time to an investigation of industrial dermatoses. These could be younger men and there could be associated with them a consulting board of mature experts in skin diseases.

Senear, Chicago.

SYPHILOMA VULVAE. Arthur Stein, Surg., Gynec. & Obst. **31**:227 (Sept.) 1920.

The descriptive term syphiloma vulvae is applied to the disease formerly named "esthiomene." Histologically, the hypertrophied masses of the diseased area are gummatous and subject to the familiar necrotic changes and cicatricial contractions seen in gummas. Clinically, the vulvar changes become manifest a long period, sometimes many years, after the primary infection. Syphilitic induration of the vulva is apt to supervene in the absence of all other specific changes after a long interval of apparent health, which accounts in part for the many mistakes in diagnosis. The treatment is both surgical and medical. Operative interference consists of excision and destructive cauterization of all tumors and excrescences. Arsphenamin intravenously is an essential supplement to the surgical treatment. Stein observed two cases at the Harlem Hospital, both in colored patients. He gives photographs of the clinical cases, and photomicrographs, also a bibliography.

Goodman, New York.

LEIOMYOMA. L. SAVATARD, Brit. J. Dermat. **32**:229 (July) 1920.

Savatard described a typical case of this rare condition. The patient, a man, aged 48, presented over the right malar region and on the external aspect of the right forearm numerous discrete nodules, varying in size from a pin head to a small berry. They varied in color from yellowish brown on the cheek and dull red on the arm, and disappeared on pressure. The nodules were firm, though of varying induration, and were movable with the skin. Some of the larger ones were very sensitive to pressure and to changes of atmosphere and temperature. Excruciating pain followed gentle manipulation of one of the larger tumors. Pain was also induced by wet weather and when the patient left a warm room. Radium and roentgen-ray therapy were without effect except that no pain had been felt in the facial lesions since the application of radium.

The microscopic picture disclosed a tumor composed entirely of smooth muscle cells. There were fine interlacing bundles of collaginous fibers in the tumor proper which gradually increased in size toward the periphery of the growth, but there was no suggestion of a fibrous capsule. No sebaceous and sweat glands or nerve filaments could be detected, but there was a hair follicle near the center of the growth. Savatard states that in his case the origin was clearly from the arrector pili.

SENEAR, Chicago.

DREI JAHRE AMTLICHER SYPHILISTILGUNG MIT SALVARSAN (THREE YEARS OF AN OFFICIAL CAMPAIGN AGAINST SYPHILIS BY USE OF ARSPHENAMIN). VICTOR L. NEUMAYER and MARIANNE NEUMAYER, Arch. f. Derm. u. Syph. **121**:820, 1916.

Rendering active syphilitics noninfectious with arsphenamin or its equivalents has markedly reduced the incidence of infection in the district of Bosnia. The mixed population of Christians and Mussulmen presented a special problem in that the Mohammedan women were at first not examined because of the religious interdiction. As a consequence the syphilitic infection reappeared in the younger children, and indeed was carried from one woman to another through the communal smoking custom. The men were, of course, infected through the women of their own household. It is interesting to note that the authors report but one case of tabes and no case of paresis in eight years' observation in this district.

GOODMAN, New York.

BEOBACHTUNGEN UEBER DIE URSACHEN DER VERSCHIEDENEN LOKALISATION DER SYPHILITISCHEN EXANTHEME (CAUSES OF VARIATIONS IN THE LOCALIZATION OF SYPHILITIC EXANTHEMS). JOHN ALMKVIST, Arch. f. Dermat. u. Syph. **123**:207, 1916.

Passive hyperemia renders a part of the body more or less susceptible to the syphilitic virus. Active hyperemia or anemia acts against the development of syphilitic changes of a portion of the body. It would appear that the relative susceptibility of the organs, not only the skin, depends in some measure on its blood distribution, in the sense of active or passive hyperemia, or anemia. It is also possible that the prognosis of a developing syphilis depends to a great measure on the state of blood distribution during the secondary stage of the disease. Other factors may of course be operative.

GOODMAN, New York.

RECKLINGHAUSEN'S DISEASE WITH SURGICAL COMPLICATIONS.

C. E. CALDWELL, Surg., Gynec. & Obst. **31**:242 (Sept.) 1920.

The conditions, fibroma molluscum, neurofibroma, and plexiform neuroma are included under the title of von Recklinghausen's disease. It is not unreasonable to assume that these conditions are dependent on some constitutional vice, probably some abnormality of the endocrine glands. Stein reports two of his cases which had complications of a surgical nature: fibroma of the ulnar nerve, degenerative changes in a large neurofibromatous mass, with accompanying neurovascular changes.

GOODMAN, New York.

CASE OF PURPURA WITH SYMMETRICAL GANGRENE OF THE FINGERS.

MAY MICHAEL, Am. J. Dis. Child. **20**:124 (Aug.) 1920.

The author reports the interesting case of a child, 2½ years old, who was taken ill with fever, restlessness, and swelling of the glands of the neck. A slight cough and sore throat were also present. During the first week of the attack large purpuric patches appeared on both upper and lower extremities; the temperature was 103.5 F. A remission occurred, during which the child seemed fairly well. During a second attack of purpura the eruption covered the trunk and extremities; this lasted six weeks. After another remission of two weeks, the first phalanges of all the fingers of the right hand, and of the thumb, index, middle and little fingers of the left hand, began to look dry and gradually turned black. After a month in the hospital, the child rapidly improved, and the purpura disappeared. The first and second phalanx of the first finger of the right hand, and the first phalanges of all the other fingers, except the thumb and left fourth finger, dropped off, but healed smoothly.

The Wassermann test was negative, and blood cultures on several occasions failed to disclose any organism. The coagulation time of the blood was normal; urine, stools and tuberculin tests were negative.

The author concluded that an infectious obliterating endarteritis—the infection being the same as that which caused the purpura—was responsible for the gangrene.

OLIVER, Chicago.

ACNE ZOSTERFORMIS.

A. BLASCHKO, Arch. f. Dermat. u. Syph. **123**: 242, 1916.

All linear dermatoses, or those that apparently follow the course of a cutaneous nerve, are not the result of local nerve disease. One must consider also anomalies of development, particularly in regard to segmental changes which result in a "locus minoris resistentiae." As a case in point, Blaschko reports the case of an 18 year old boy, in whom a general examination disclosed along the course of the seventh dorsal nerve left of the spinal column an area about palm sized, with numerous, thickly aggregated, black-headed comedones. A smaller group was situated in the mammary line of the same nerve, and still two smaller groups of three or four comedones at the lateral and midlines. No other comedones were in the area immediately adjoining. The case reminded Blaschko of nevus acneiformis, but the history disclosed that the patient had recently recovered from an attack of true zona and that the comedones first appeared after the regression of that disease. Apparently, some structural changes had occurred that were favorable to the development of comedones.

GOODMAN, New York.

USE OF QUARTZ LIGHT IN DERMATOLOGY. E. L. Oliver, Boston M. & S. J. **183**:155 (Aug. 5) 1920.

This article gives a short history of the development of the quartz light and a discussion of its physics. The author states that the effect produced by sunlight and this light are identical; that the efficiency of treatment with the light is dependent on the dosage, and that most of the unfavorable results in certain types of cases are due to insufficient treatment. Comparatively little discomfort is produced by the erythema or by the blister if the Kromayer lamp is used.

In twenty-five cases of varicose ulcer, almost without exception improvement was more rapid than would be expected from other methods of treatment. The light treatment has given results more rapidly, has relieved the pain, has kept the patient on his feet, and the new epithelium has been thicker and firmer, and more nearly like normal skin. Exposures to the Alpine sun lamp, usually about two minutes at a distance of 10 inches, have been sufficient to produce a distinct erythema of the skin about the ulcer. The treatment was repeated every week and the time of exposure increased gradually.

Flat vascular nevi have also been successfully treated by pressure with the Kromayer lamp. Fifty per cent. improvement after a single treatment is not unusual. The amount of fading of these lesions on pressure is a valuable measure in evaluating the result. Incidentally the author gives a word of warning against the too free use of radium in portwine marks because of subsequent changes in the skin. Alopecia areata often responds very favorably. In other types of alopecia its use is doubtful. In chronic patches of psoriasis, especially of the nails, in resistant patches of chronic eczema, and in a few cases of pruritus ani and pustular acne vulgaris it proved of value. Its availability, time saving, and ease of application are emphasized as advantages of the quartz light over natural sunlight.

Lane, Boston.

[Note.—Of course, many other competent workers have failed to get such favorable results with the Kromayer lamp, notably in nevus.—Ed.]

EIN BEITRAG ZUM KAPITEL: DERMATOLOGISCHE KRIEGSERFAHRUNGEN (WAR EXPERIENCE IN DERMATOLOGY). J. F. von Crippa, Arch. f. Dermat. u. Syph. **123**:285, 1916.

Self inflicted dermatologic lesions were not unknown among the German forces. The means employed and diseases simulated were those of other countries. Natural skin diseases were made worse or healing disturbed. It is interesting to note that Crippa is certain that the German troops were less subject to these practices than those of their opponents, for example, the English. [On the other hand, Davis (Dermatitis Artefacta in the Army, *Arch. Dermat. & Syph.* **2**:82, 1920) says that there were few cases in the British Forces.]

Goodman, New York.

ACTINOMYCOSIS OF THE LOWER LIP. John R. Harger, Surg., Gynec. & Obst. **31**:305 (Sept.) 1920.

Harger presented a case before the Chicago Surgical Society. Microscopic section disclosed the ray fungus.

Goodman, New York.

NOCHMALS ZUR KLINIK UND ZUR STELLUNG DES "BENIGEN MILIARLUPOIDS" (CLINICAL STUDY AND CLASSIFICATION OF BENIGN MILIARY LUPOID). C. Boeck, Arch. f. Derm. u. Syph. **121**:707, 1916.

Multiple benign sarcoid is clinically and histologically a constitutional bacillary infection, which is probably a distinct but mild type of tuberculosis. The excitant of the disease, which tinctorially and morphologically is indistinguishable from the bacillus of Koch, is demonstrable in the sections of the vegetating but not the ulcerating mucosa of the nasal passages. Inoculation of guinea-pigs has given characteristic results.

Goodman, New York.

ARSPHENAMIN AND NEO-ARSPHENAMIN. W. A. Smith, J. Lab. & Clin. M. **5**:518 (May) 1920.

Smith gives a brief résumé of the origin, present supply and rules for manufacture of these therapeutic agents. In the technic of administering the drugs, nothing new of importance is mentioned. Reactions and their causes, also the use of the preparations in treatment are discussed, and a number of references to the literature are added. In his discussion of the comparative value of the two preparations, the author quotes freely from Schamberg's recent articles showing that neo-arsphenamin is two and one-half times less toxic for white rats than the arsphenamin from which it is made. Arsphenamin was tolerated at 100 mg. per kilogram of body weight, while the neo-arsphenamin was tolerated at 250 to 300 mg. per kilogram. Arsphenamin in practically all concentrations hemolyzes red blood cells in vitro; neo-arsphenamin does not do so in any concentration normally used.

Arsphenamin is more curative than the neo-arsphenamin. Schamberg found that to sterilize rats experimentally infected with *Trypanosome equiperdum* (horse syphilis) it took twice as much of neo-arsphenamin as of arsphenamin. The arsenic content of three parts of neo-arsphenamin equals that of only two parts of arsphenamin. Schamberg thus concludes that the arsphenamin is more active therapeutically, but this difference is made up by the discrepancy in tolerated dosage, as 0.9 gm. of neo-arsphenamin can be given three times a week. Neo-arsphenamin creates much less biochemic disturbance in the blood and tissues.

Waugh, Chicago.

TREATMENT OF ANGIOMAS WITH RADIUM. William S. Newcomet, Am. J. Roentgenology **7**:337, 1920.

In radium, as in the roentgen ray, we have an agent that is capable of doing considerable harm under some circumstances; therefore it must be employed with great care, especially when it is impossible to judge exact dosage. It should be remembered that as a rule people live in the present and to a great extent forget the past. Therefore, if a scar or slight discoloration remains, it may be judged a bad result with no regard for the former condition even if it should have been repulsive.

The amount usually given is about an erythema dose, which must be judged according to the applicator used, the filter and the skin distance. The last factor is by far the most important and varies according to the depth of the nevus. If it is deep, the applicator is placed from 3 to 6 cm. away and moved frequently to produce "cross-fire" effect. The tubes are used exclusively. The skin bordering the nevus must be protected, and if filters are used, they should extend slightly over the edge of the nevus rather than expose the skin.

Goodman, New York.

GENERALISIERTE HAUTOEDEME BEI UNIVERSELEM EKZEM (GENERALIZED CUTANEOUS EDEMA IN UNIVERSAL ECZEMA).

H. Fuchs, Arch. f. Derm. u. Syph. **121**:947, 1916.

A woman patient, aged 53, gave a history of having had a chronic eczema of the body for three years. The condition was relieved, and she was referred to the outpatient department. A universal edema set in, but the consistency was varied in different parts of the body. There was no evidence of heart or kidney disease. She rapidly gained 5 kg. despite treatment of all kind. She left the hospital at her own request. The follow up history stated that the edema had improved, but that the patient had lost weight and strength through a profuse diarrhea and had died. At no time during her illness was albumin detected in her urine. Fuchs believes that the eczema was the direct cause of the edema.

Goodman, New York.

LUES UND TUBERCULOSIS VERRUCOSA CUTIS (SYPHILIS AND TUBERCULOSIS VERRUCOSA CUTIS).

H. Fuchs, Arch. f. Derm. u. Syph. **121**:955, 1916.

Three patients presented symptoms of their syphilitic infection which so closely resembled the picture of tuberculosis verrucosa cutis, that the diagnosis could not be made on clinical evidence alone.

Goodman, New York.

NOMA IN THE DOG.

J. McJ. Phillips and Fred Berry. J. Infect. Dis. **27**:136 (Aug.) 1920.

A case is reported of a dog, 9 months of age, which after a mild attack of distemper, developed an ulcerative condition of the mouth similar in every respect to noma. Smears showed equal numbers of fusiform bacilli and spirilla. A majority of smears from the gums of a number of normal dogs in the same kennel contained B. fusiformis and spirilla, usually in small numbers. The occurrence in a dog of a noma so similar to that in man, makes it appear possible that the dog may be a source of infection to man, especially to persons recovering from acute diseases, who are more susceptible to such infection.

Oliver, Chicago.

NAEVI ANAEMICI UND RECKLINGHAUSENSCHE KRANKHEIT (ANEMIC NEVUS AND RECKLINGHAUSEN'S DISEASE).

O. Naegeli, Arch. f. Derm. u. Syph. **121**:742, 1916.

Two patients presented a combination of von Rechlinghausen's disease and nevus anemicus. Probably more cases of this association have not been reported because the nevus has been mistaken for vitiligo.

HAUTALLERGIE BEI GONORRHOE. VERSUCHE MIT NEISSERSCHER GONOKOKKEN-BOUILLON (SKIN ALLERGY IN GONORRHEA. EXPERIMENTS WITH NEISSERIAN GONOCOCCUS BOUILLON). H. Fuchs, Arch. f. Dermat. u. Syph. **123**:331, 1916.

The intradermal injection of gonococcus bouillon excites in the majority of patients suffering with gonococcal infections a skin allergy that is not found in healthy persons. This allergy persists for several months after the disease has regressed, and does not depend on the clinical form of the disease. Ordinarily the phenomenon is first seen six days after infection. It is possible by means of this reaction to distinguish sequels that are dependent on the gonorrheal infection from those that are not.

VERTAEUSCHUNG EINES SYPHILITISCHEN PRIMAERAFFEKTES DURCH EINE NACH ORTHOFORMBEHANDLUNG EINER RHAGADE IM SULCUS CORONARIUS PENIS ENSTANDENE NEKROSE (NECROSIS AFTER ORTHOFORM TREATMENT OF RHAGADES OF THE CORONARY SULCUS OF THE PENIS SIMULATING PRIMARY CHANCRE). Otto Sachs. Wien. klin. Wchnschr. **33**:680, 1920.

A physician substituted orthoform for xeroform as a local application to coronal rhagades. The resulting clinical picture simulated a primary syphilitic lesion. Sachs reviews the use of orthoform and submits a bibliography.

DIE PIGMENTIERUNGEN DER HAUT BEI PERNIZIOESER ANAEMIE (CUTANEOUS PIGMENTATION IN PERNICIOUS ANEMIA). T. Schucany, Arch. f. Derm. u. Syph. **121**:746, 1916.

The study of the skin histologically of two cases of pernicious anemia and one of hemachromatosis, which clinically presented similar pigmentation, revealed a typical Addison pigmentation, a marked arsenmelanose, and an extensive deposition of hemosiderin. It appears that the skin changes in pernicious anemia are not of a single nature, and that for specific diagnosis, histologic examination of the skin is essential.

UEBER EINEN FALL VON PARAPSORIASIS (CASE OF PARAPSORIASIS). Muschter, Arch. f. Derm. u. Syph. **121**:918, 1916.

A case of parapsoriasis is reported which shows the three clinical types of the disease. This is the second case of the kind to be reported in the literature. The author is of the opinion that the three clinical types of the disease that have been described are not clinical entities but varieties of the same affection. He does not concur with Werther in naming the disease "pityriasis lichenoides chronica polymorpha."

ABNORMES HAARWACHSTUM NACH TIEFER TRICHOPHYTIE DES KOPFES (ABNORMAL GROWTH OF HAIR AFTER DEEP TRICHOPHYTOSIS CAPITIS). H. Fuchs, Arch. f. Derm. u. Syph. **121**:945, 1916.

Following roentgen-ray depilation and the use of mercury salve for tinea of the scalp, a boy of 9 years returned to the clinic presenting a most curious new growth of hair. Areas that formerly were diseased showed a heavier and darker growth than the former normal areas.

DER LICHEN SCLEROSIS (LICHEN SCLEROSUS). Arthur Alexander, Arch. f. Derm. u. Syph. **121**:925, 1916.

Alexander describes two cases that are identical with lichen sclerosus (Hallopeau) yet whose lichen characters are so marked and distinguished that they clinically present no similarity to either scleroderma or white spot disease.

UEBER EINEN FALL VON HYPERKERATOTISCHEM EXANTHEM BEI GONORRHOE UND LUES (CASE OF HYPERKERATOSIS WITH GONORRHEA AND SYPHILIS). Ernst Nathan, Arch. Derm. u. Syph. **121**:906, 1916.

A clinical and histologic presentation of this rare affection described for the first time in a patient with secondary syphilis and gonorrheal urethritis.

UEBER URTIKARIA UND URTIKARIELLE EXANTHEME (URTICARIA AND URTICARIAL EXANTHEMS). G. Scherber, Archiv f. Derm. u. Syph. **121**:765, 1916.

This article presents a critical review of the urticaria syndromes.

Goodman, New York.

Book Reviews

MANUAL OF TROPICAL MEDICINE. By Aldo Castellani, C.M.G., M.D., M.R.C.P., Lecturer at the London School of Tropical Medicine, and Albert J. Chalmers, M.D., F.R.C.S., D.P.H., Director, Wellcome Tropical Research Laboratory (Soudan Government). Third Edition. Pp. 2437. New York: William Wood & Co., 1919.

The third edition of Castellani and Chalmers' "Tropical Medicine" presents to us in enlarged form a work that is of the greatest value to dermatologists. It is valuable for its account of skin diseases in the tropics, but its greatest value lies in the systematic and exact exposition of the subject of the vegetable and animal parasites that attack the skin. In this field it is a reference book which the reviewer has in the past found invaluable. One cannot but admire to the highest degree the thoroughness with which these subjects have been covered.

Not less than 270 pages are devoted to the section on skin diseases, not including such important diseases as yaws, verruca peruana, leprosy and pellagra, which are treated under general diseases, nor the parasitology of skin diseases, which is a part of the general consideration of parasitology. This amount given to skin diseases is testimony to their importance in the tropics, and to the authors' familiarity with and interest in them. In the part devoted to skin diseases are considered not only many interesting infections unknown to us, but there are also descriptions of many familiar conditions in new guises as they appear in the tropics. Indeed, one is inclined to feel that many of the diseases which are described as new, or by new names, are familiar diseases intensified by tropical conditions. The only criticism which the dermatologist is likely to make of the book lies in this direction. There are undoubtedly many new names given to known affections. The authors apparently are rather ready to describe new conditions, especially those due to new species of vegetable parasites.

This new edition as a whole is a colossal work; it contains 2436 octavo pages and it is modestly called a manual! It ought to be in at least two volumes, for the single volume is unwieldy in size and weight, and cannot long hold together under much use. It is a veritable thesaurus of facts about the tropics and its diseases: The History of Tropical Medicine, Tropical Races, Tropical Climatology, Tropical Foods, Tropical Diseases, Fitness for Tropical Life—these are the chapter headings of the 127 pages of Part I, the introduction. Part II considers the Causation of Disease in the Tropics, and Part III, The Diseases of the Tropics. The whole of it is interesting reading.

The work is a monument to the industry, scientific zeal, and comprehensive scholarship of its authors. It is a great book.

SYPHILIS DE L'UTERUS ET DE SES ANNEXES (SYPHILIS OF THE UTERUS AND ADNEXA). E. Ozenne, Paris, Masson et Cie, 1920.

Ozenne has produced an excellent monograph on syphilis of the uterus and adnexa, including the mammary glands. The volume is worth a rapid perusal in order to glean the essentials of the contents, but it would be a worthy addition to any library for reference, for it contains a wealth of detail, carefully assembled and clearly arranged. The bibliography is extensive, and the arrangement of the text is so simple and expository that it enhances the volume in the eyes of readers fancying the method of direction. The divisions of the book are: syphilis of the uterus, syphilis of the adnexa and syphilis of the breasts. Each division contains subsections devoted to the several stages of the disease, with a particularly valuable passage at the end of the first division on syphilis of the gravid uterus.

Some of the most striking points the author brings out are: In discussing the incidence of chancre of the cervix, he hints that it is found in this situation more frequently than elsewhere, but is not recognized partly because it resembles cancer, but more because by the time the patient presents herself the lesion is healed. When gravidae have primary syphilis the lesion is frequently found on the cervix, generally on the anterior lip.

There is a splendid description of the secondary and tertiary lesions of the cervix and of these phases of the disease in the uterine body, including both the symptoms and signs. Often gummas of the body of the uterus simulate in all clinical respects fibromyomas. There is an illuminating reference to the effect of syphilis on the gravid uterus, with particular consideration of dystocia due to primary cervical lesions, and the questions of the mechanism of miscarriage.

Syphilis of the tubes takes the form of salpingitis of different grades of severity, and gummas, according to the stage of the disease. Secondary ovaritis is likened to epididymitis, and gummas may develop with the symptoms of tumors or cysts. Mammary syphilis is reduced to a matter of recognizing primary and tertiary lesions, particularly the latter, because of their resemblance to tumors.

The book is undoubtedly a signal contribution to the clinical knowledge of syphilis. It is a pity that physicians have not the leisure to create a larger number of such monographs, for their place as reference sources cannot be exaggerated. Such works indicate a sort of scientific patriotism, for they represent untold drudgery, and are thus doubly to be commended.

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THE RESISTANCE (OR IMMUNITY) DEVELOPED BY THE REACTION TO SYPHILITIC INFECTION

AND SOME OF THE EFFECTS OF THE SUPPRESSION OF THIS REACTION *

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NEW YORK

The idea of an inhibitory influence has been suggested as a means of explaining certain phenomena of syphilitic infections and there is some experimental evidence on which to base such a conception. The difficulty has been that most of the evidence cited in support of this theory was susceptible of more than one interpretation. This applies in particular to reinoculation and superinfection experiments which have been the favorite means of demonstrating inhibitory effects. Nowhere, however, is the action of such an influence more strongly suggested than in the experimental infection produced in the rabbit by scrotal or testicular inoculations of well adapted strains of *Spirochaeta pallida.*

As it is ordinarily seen, the two most striking features of this infection are an extremely marked reaction at the site of inoculation and a total absence of generalized manifestations of disease. If one considers these peculiarities of the experimental infection as compared with that in man, one can hardly fail to see a possible connection between the two conditions mentioned, especially when it has been shown that the absence of generalized lesions in the rabbit cannot be accounted for either by a lack of dissemination of spirochetes or by a tissue insusceptibility.

It appeared to us that the reaction to infection as it occurred in the rabbit offered an opportunity for determining the influence which a syphilitic reaction in one part of the body might exert on manifestations of the disease elsewhere and, at the same time, a possibility of modifying the experimental infection so as to increase its usefulness as a means of investigating problems of human syphilis.

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Accordingly, a series of experiments was carried out with a view to determining the effect which a simple reduction or suppression of the reaction at the site of inoculation might have on other clinical manifestations of the infection.

EXPERIMENTAL

The means employed in making these comparisons were unilateral as contrasted with bilateral inoculation, unilateral and bilateral castration at various stages of the infection, suppression of the primary reaction by the use of therapeutic agents and complete prevention of a primary reaction. (Castrations were made under ether anesthesia.)

The effects produced were gaged on the basis of the occurrence of generalized lesions. In the rabbit, the conditions which one may recognize clinically include various forms of cutaneous lesions, lesions of the mucous membranes, lesions of the periosteum and bones, lesions of the eyes and a general lymphadenitis. The latter condition is of such common occurrence, even when no other clinical sign of generalized infection can be recognized, that it was not used as a standard of comparison.

The results obtained from these experiments will not be reported in detail, but the essential character of the effects produced by the procedures indicated will be given briefly.

EFFECTS OF UNILATERAL AND BILATERAL INOCULATION AND OF CASTRATION

In the first group of experiments, a comparison was made of the effects of unilateral and bilateral inoculation and of the removal of the infected testicles soon after the appearance of the initial lesions. The results of these procedures were determined on the basis of a period of four months' observation.

Bilateral Inoculations.—Of twenty rabbits inoculated in both testicles, fourteen were castrated and six were held as controls. Generalized lesions developed in one of the six controls and in thirteen of the fourteen castrated animals within the period of observation.

Unilateral Inoculations.—Twenty-seven rabbits were inoculated in one testicle only; fourteen of these were castrated and thirteen were held as controls. In this series, generalized lesions developed in eight of the thirteen controls as contrasted with one of six animals inoculated in both testicles and again in thirteen of the fourteen castrated animals.

Several other experiments of a similar character gave essentially the same results, thus showing that by inoculating one testicle instead of two, the incidence of generalized lesions was markedly increased.

When the reaction at the site of inoculation was further reduced by early removal of the infected organs, generalized lesions developed in almost every instance.

EFFECTS OF SUPPRESSION OF PRIMARY LESIONS BY THERAPEUTIC AGENTS

In a second set of experiments in which castrations were made at different stages of the infection, the effects of suppression of the testicular lesion by the use of a therapeutic agent was also tested. For this purpose, a drug was chosen from among those studied by us in collaboration with Dr. W. A. Jacobs and Dr. Michael Heidelberger, whose effect in inducing resolution of syphilitic lesions was much greater than its spirocheticidal action. This substance was arsenophenylglycyl dichloro-m-aminophenol.

Twelve rabbits, six of them inoculated unilaterally and six bilaterally, were given a single intravenous injection of this drug (5 mg. per kilo) fourteen days after inoculation, and the results were controlled by six untreated rabbits from each of the respective groups.

In the unilateral series, the lesions present were almost completely resolved and the local reaction suppressed for between two and three weeks. At the end of three months, all of these animals had developed generalized lesions as contrasted with three of the six controls. The effect of the drug on the animals inoculated in both testicles was less marked and lasted for only from seven to ten days. At the end of three months, generalized lesions had developed in four of the six treated animals and in one of five surviving controls.

This experiment showed that by properly gaging the dose of a therapeutic agent so as to suppress the lesions present without destroying the infecting organisms, the infection can be intensified in the same way as by an excision of the primary lesions.

EFFECTS OF COMPLETE PREVENTION OF A REACTION AT THE SITE OF INOCULATION

In another experiment, the reduction of the reaction at the site of inoculation was carried to the point of complete prevention. This was accomplished by inoculating ten rabbits in the right scrotum, using tissue implants, and at the end of forty-eight hours completely excising the scrotum and testicle of that side under ether anesthesia.

By the end of the seventh week, eight of the ten rabbits in this series showed a marked generalized syphilis and the other two developed slight generalized lesions at the end of two and two and one-half months.

Taken as a whole, the generalized infection in this series of animals was the most pronounced which we have seen in any single group of rabbits. This would indicate that both the incidence and severity of the generalized infection tend to increase in proportion to the reduction or suppression of the reaction at the site of inoculation.

CONCLUSION

These experiments show that, in so far as syphilitic infections in the rabbit are concerned, the reaction which takes place at the site of inoculation tends to dominate the entire course of the infection; that, in effect, this reaction either inhibits or obviates the necessity for the development of lesions elsewhere and, conversely, that the reduction or suppression of the reaction by the use of any means that does not exercise an equal effect on the organisms themselves, removes this control and tends to increase the occurrence of generalized lesions and the severity of the infection.

If one is prepared to accept the infection produced in the rabbit by *Spirochaeta pallida* and the reaction to infection on the part of the experimental animal as analogous in kind to those in man, these observations become of far reaching importance and may open the way to a better understanding of many problems of human syphilis.

PROVOCATIVE REACTIONS IN THE CEREBROSPINAL FLUID IN NEUROSYPHILIS *

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The provocative arsphenamin reaction in the blood is a familiar phenomenon. In many clinics, when a patient suspected of having syphilis gives a negative Wassermann reaction, an injection of arsphenamin is given; then the blood is tested at daily intervals thereafter, because it apparently has been shown that after the injection of arsphenamin the Wassermann reaction will be positive in some cases.

It is our purpose to call attention to a similar reaction taking place in the spinal fluid. We report several cases in which, after either intravenous or intraspinal injections, a negative spinal fluid became positive, or the positive pathologic findings were intensified. From the clinical standpoint, the phenomenon of intensification of symptoms relating to the central nervous system has frequently been described as occurring after treatment. To this phenomenon the term neurorecidive or neurorecurrence has been applied. One is not sure in these cases whether the resulting intensification of symptoms is due to the introduction of the drug or whether it is a mere coincidence that an increase of symptoms appears following the injection. However, in relation to secondary syphilis, the intensification of symptoms following arsphenamin injection has occurred so frequently that it has been considered as due to liberation of toxins resulting from the lytic action of arsphenamin on the spirochetes. This is the so-called Herxheimer reaction. If this can occur in skin lesions, there is every

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reason to suppose, a priori, that the same thing may occur in neurosyphilis. However this may be, the following cases would appear to show that following intravenous and intraspinal injections of arsphenamin or arsphenamized serum, the spinal fluid findings may become more strongly positive.

REPORT OF CASES

CASE 1.—*History.*—F. H., aged 36, according to the history obtained from the patient, had experienced a sudden paralysis of the right leg and arm about eighteen months previous to his admittance to the clinic. He recovered from this in about two days. At the time his physician gave him a liquid medicine (potassium iodid?). During the three months preceding his admittance to the clinic he had been receiving intramuscular injections of mercury. He denied syphilitic infection, but admitted exposure. He also admitted excessive use of alcohol. He had been married five years. His wife was living and well, but had never been pregnant. At the time of admittance he complained of headaches, some loss of memory and a mild speech defect at times. The visceral examination revealed nothing abnormal.

Examination.—Neurologic: The pupils were equal and reacted to light. The left patella and biceps reflexes were more active than the right. Abdominal and cremasteric reflexes were normal. There were no abnormal reflexes. Muscle strength in the legs and arms was good. Station and gait were normal. Ophthalmoscopic examination showed a few vitreous opacities, but the disk and choroid were normal.

Mentally he seemed somewhat euphoric, boasting with great confidence of his abilities. No definite memory disorder or speech defect was noted.

The Wassermann reaction was negative on the blood and spinal fluid; the other spinal fluid tests, including cell count, globulin, albumin, and colloidal gold reaction, were negative.

There was a difference of opinion as to the diagnosis, some members of the staff diagnosing the case as neurosyphilis despite the negative laboratory findings. Because of this difference of opinion, the patient was given a provocative injection of arsphenamin. The blood was drawn at intervals of twenty-four, forty-eight and seventy-two hours after the injection; all tests were reported as negative. The spinal fluid was drawn some time later and gave the following reactions: Wassermann reaction positive with 1 c.c. and 0.8 c.c.; negative with 0.6 c.c. and with the higher dilutions. There were 53 cells per cubic millimeter; globulin was present; and albumin was present in excess. The colloidal gold reading was 244333000.

We may assume then, that a provocative reaction in the spinal fluid occurred as a result of the intravenous injection of arsphenamin, the reactions which had previously been negative becoming positive. This provocative reaction did not appear in the blood.

Blood and Spinal Fluid Reactions.—The following reactions were obtained before treatment: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, negative. After one intravenous injection of arsphenamin was given the reactions obtained were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 55 — — — — — (positive);[1] globulin, 2; albumin, 2; cells, 53 per cubic millimeter; colloidal gold curve, 2443330000.

Case 2.—*History.*—This patient came under observation in the routine follow-up of the families of our known syphilitic patients. His wife was suffering from general paresis. Both denied any history of infection, although some years before a stillbirth had led to a diagnosis of syphilis, and a small amount of treatment had been given to both husband and wife.

Examination.—When examined the patient was in good health, and the only significant symptom was an inequality of the pupils. The Wassermann reaction of the blood was negative, but in view of the inequality of the pupils, a lumbar puncture was performed. This showed a Wassermann reaction positive with 1 c.c. of fluid, but negative with the higher dilutions. Globulin was absent; albumin was present in normal amounts; there were 9 cells per cubic millimeter and the colloidal gold reaction was negative. This test was repeated with similar results. Six injections of arsphenamin were then given over a period of some months. Five months later another spinal fluid examination was made. This again gave a positive Wassermann reaction with 1 c.c., 0.7 c.c., and 0.5 c.c. of spinal fluid. No cells were found in the specimen examined. Globulin was not obtained, and the albumin was present in normal amounts. The colloidal gold reaction was again negative. Thirteen injections of arsphenamin were given in the next ten months, and a spinal fluid examination at this time showed a positive Wassermann reaction with 1 c.c., 0.7 c.c., and 0.5 c.c. of spinal fluid. Globulin was present; there was an increase of albumin; and a pleocytosis of 25 cells per cubic millimeter was found. The colloidal gold reaction gave a strong paretic curve, reading 5554443211.

Treatment and Course.—In the following eleven months, twenty-four injections of arsphenamin were given. At this time, the spinal fluid gave a doubtful Wassermann reaction, that is, there was a partial inhibition of hemolysis with 1 c.c. of spinal fluid, 0.8 of a c.c. giving a negative reaction. There were 4 cells per cubic millimeter; globulin was present in small amounts, and albumin was slightly increased. The colloidal gold reading was 1143210000, a reaction typical for cerebrospinal syphilis. The patient was given an injection of arsphenamin, and an intraspinal injection of Swift-Ellis serum, fortified by ⅓ mg. of arsphenamin. Two weeks later, another specimen of spinal fluid was examined. The Wassermann test was not made. The cell count was normal. There was a slight amount of globulin, and a small increase in the albumin. The colloidal gold reaction was 1112100000, an almost negative reaction. This examination was followed by two injections of arsphenamin and one intraspinal injection similar to the previous one.

Blood and Spinal Fluid Reactions.—The reactions obtained Aug. 17, 1917, before treatment were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 5 — — — — — — (positive); globulin, 0; albumin, normal; cells, 9 per cubic millimeter; colloidal gold test, negative. After six intravenous injections of arsphenamin the reactions obtained Jan. 18, 1918, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 5541 —— (positive); globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, negative. After fourteen intravenous injections of arsphenamin the reactions obtained Nov. 9, 1918, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 555000 (positive); globulin, +; albumin, + +; cells, 25 per cubic millimeter; colloidal gold test, 5554443211. After twenty-six intravenous injections of arsphenamin the reactions obtained Oct. 21, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 3—0000 (doubtful); globulin, +; albumin, + +; cells, 4 per cubic millimeter; colloidal gold test, 1143210000. After two intravenous injections of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained Nov. 8, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, unsatisfactory; globulin, +; albumin, +; cells, 2 per cubic millimeter; colloidal gold test, 1112100000. After three intravenous injections of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained Dec. 16, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 28 per cubic millimeter; colloidal gold test, 5445410000. After six intravenous injections of arsphenamin the reactions obtained April 17, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 5 per cubic millimeter; colloidal gold test, 3333320000. After two intravenous injections of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained May 4, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 2; albumin, 1; cells, 4 per cubic millimeter; colloidal gold test, 5555531000.

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[1] The Wassermann reaction on the spinal fluid is performed on titrated quantities varying from 1 c.c. to 0.05 c.c. The figure 5 represents strongly positive and a dash (—) a negative reaction. Each figure or dash represents the reaction for a certain dilution, the figure at the left representing the reaction with 1 c.c. of fluid, the second figure in 0.8 c.c., the third in 0.6 c.c. and so on in diminishing amounts. When a zero occurs it means that the test was not made in the dilution represented by its position.

Case 3.—*History*.—This patient was seen first in the ataxic state of tabes dorsalis. He gave no history of syphilitic infection, but had been complaining of weakness in the legs and general malaise for about two years. He had been given twelve intravenous injections of arsphenamin at a local dispensary.

Examination.—This showed a classic picture of advanced tabes dorsalis. The pupils were unequal and gave the Argyll Robertson reaction. There was a paresis of the left external rectus muscle. Knee jerks and ankle jerks were absent. The patient was practically bedridden. The Wassermann reaction was negative for the blood and spinal fluid. There were 5 cells per cubic millimeter in the spinal fluid, a slight amount of globulin, and a slight increase of albumin. The colloidal gold reaction was essentially negative, 0000110000.

Treatment and Course.—He was given an intraspinal injection of Swift-Ellis serum, reinforced by 0.0002 gm. of arsphenamin, and one intravenous injection of arsphenamin. The spinal fluid examination two weeks later gave a positive Wassermann reaction down to 0.3 of a c.c. Globulin was absent; albumin was present in normal amounts; there were 3 cells per cubic millimeter, and the colloidal gold reaction was again essentially negative, 0001200000. Another intraspinal injection of the same type as the previous one and four intravenous injections of arsphenamin were given, and in six weeks the spinal fluid was again examined. The Wassermann reaction was doubtful; a slight amount of globulin was present; albumin was increased; there were 3 cells per cubic millimeter, and a fairly strong colloidal gold reaction, 4432210000. Another intraspinal injection of Swift-Ellis serum, reinforced by 0.0001 gm. of arsphenamin and five intravenous injections of arsphenamin were given, and five weeks later the spinal fluid showed a positive Wassermann reaction with 0.5 of a c.c.; one cell per cubic millimeter; globulin was present; albumin was increased; and a colloidal gold reaction of 4333210000 was obtained. The intraspinal treatment was repeated, reinforcement of arsphenamin being by 0.0003 gm., and another fluid examination was made three weeks later. The Wassermann test was positive with 1 c.c. and moderately positive with 0.7 c.c. and 0.5 c.c. There were 9 cells per cubic millimeter; globulin was present; albumin was increased; the colloidal gold reaction was 4433210000. In the following two months, two further intraspinal treatments were given of the same type as the last, and the spinal fluid again showed a positive Wassermann reaction with 1 c.c. and 0.7 c.c., and doubtful reactions with 0.5 c.c. and 0.3 c.c. There were 6 cells per cubic millimeter; globulin was present; albumin was increased; and the colloidal gold reaction was 1123100000.

Blood and Spinal Fluid Reactions.—The reactions obtained before treatment, June 7, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 5 per cubic millimeter; colloidal gold test, 0000111000. After one intraspinal injection of arsphenamized serum and one intravenous injection of arsphenamin the reactions obtained, June 21, 1919, were: Wassermann reaction of the spinal fluid, 55555— (positive); globulin, 0; albumin, normal; cells, 3 per cubic millimeter; colloidal gold test, 0001200000. After one intraspinal injection of arsphenamized serum and four intravenous injections of arsphenamin the reactions obtained, Aug. 2, 1919, were: Wassermann reaction of the spinal fluid, doubtful; globulin, +; albumin, +; cells, 3 per cubic millimeter; colloidal gold test, 4432210000. After one intraspinal injection of arsphenamized serum and five intravenous injections of arsphenamin the reactions obtained, Sept. 9, 1919, were: Wassermann reaction of the spinal fluid, 5551—— (positive); globulin, +; albumin, +; cells, 1 per cubic millimeter; colloidal gold test, 4333210000. After one intraspinal injection of arsphenamized serum the reactions obtained, Sept. 27, 1919, were: Wassermann reaction of the spinal fluid, 543——— (positive); globulin, +; albumin, +; cells, 9 per cubic millimeter; colloidal gold test, 4432210000. After three intraspinal injections of arsphenamized serum the reactions obtained, Nov. 21, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 5532—— (positive); globulin, +; albumin, +; cells, 6 per cubic millimeter; colloidal gold test, 1123100000. No treatment was given. The reactions obtained, Dec. 13, 1919, were: Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 2 per cubic millimeter; colloidal gold test, 3432210000. After one intravenous injection of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained, Jan. 11, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 4————— (doubtful); globulin, 0; albumin, 0; cells, 4 per cubic millimeter; colloidal gold test, 1111100000. After one intravenous injection of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained, Feb. 21, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, 1; cells, 5 per cubic millimeter; colloidal gold test, 1122100000. After one intravenous injection of arsphenamin and one intraspinal injection of arsphenamized serum the reactions, March 20, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 4 per cubic millimeter; colloidal gold test, 1123210000. After one intraspinal injection of arsphenamized serum the reactions obtained, April 17, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 7 per cubic millimeter; colloidal gold test, 2210000000. After two intravenous injections of arsphenamin and two intraspinal injections of arsphenamized serum the reactions, June 12, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, normal; cells, 2 per cubic millimeter; colloidal gold test, negative.

CASE 4.—*History.*—This patient gave a history of a chancre twenty years ago, which was burned with caustic. No secondary symptoms appeared, and he had no further treatment. Nothing of importance occurred until six months ago, when he began to feel dizzy, complained of sharp, shooting pains in the right arm and leg and severe frontal headache, which kept him awake at night. He was also quite dizzy. A short time later he had an attack, which left him weak on the right side, and about a month later his speech became thick. Impotence came on about this time. He went to a local dispensary where he was given fourteen injections of arsphenamin at weekly intervals. When seen by us, he was complaining of about the same symptoms, except that his dizziness was less marked and his headache had disappeared. In addition, he had difficulty in swallowing, "things going down the wrong way," and he was short of breath.

Examination.—The pupils were small, about equal in size and reacted sluggishly to light. There was no nystagmus or strabismus and no diplopia. The right side of the face was drawn up slightly. The tongue protruded in the midline. The right half of the palate was not raised as well as the left. There was a dysarthria; test phrases were pronounced a little heavily and with slurring. The arm reflexes were sluggish, but the right reflex was more pronounced than the left. The knee jerks and ankle jerks were absent. The patient walked with a slight ataxia, and there was marked swaying in the Romberg position. There was subjective numbness of the right hand but no objective sensory disorder. The Wassermann reaction was negative for the blood and spinal fluid. There were no cells in the cubic millimeter of fluid examined; globulin was not present; albumin was present in normal amounts; the colloidal gold reaction was essentially negative, 0000001110.

Course and Treatment.—He was given an intraspinal injection of Swift-Ellis serum, reinforced by 0.0002 gm. of arsphenamin, and five intravenous injections of arsphenamin. The spinal fluid examination, six weeks after the intraspinal injection, showed 13 cells per cubic millimeter. Globulin was present; albumin somewhat increased, and there was a paretic colloidal gold reaction, 5555431000. The Wassermann reaction on the spinal fluid was not done. He was given another intraspinal injection and four intravenous injections. The Wassermann reaction was negative; globulin was present in small amounts; albumin was increased; and the colloidal gold reaction was 5444321000. Another intraspinal injection of Swift-Ellis serum, reinforced by 0.0005 gm. of arsphenamin, was given, and five weeks later the spinal fluid was again examined, showing a negative Wassermann reaction; 1 cell per cubic millimeter; globulin was present; albumin was increased, and the colloidal gold reaction was 5433211000. There had been no subjective improvement in the patient, consequently treatment was discontinued for a time. At the end of two months, the patient had a shock resulting in hemiplegia.

Blood and Spinal Fluid Reactions.—The reactions obtained before intraspinal treatment, June 14, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, 0000001110. After one intraspinal injection of arsphenamized serum and four intravenous injections of arsphenamin the reactions obtained, Aug. 2, 1919, were: Wassermann reaction of the spinal fluid, not reported; globulin, +; albumin, +; cells, 13 per cubic millimeter; colloidal gold test, 5555431000. After one intraspinal injection of arsphenamized serum and four intravenous injections of arsphenamin the reactions obtained, Sept. 6, 1919, were: Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 1 per cubic millimeter; colloidal gold test, 5444321000. After one intraspinal injection of arsphenamized serum and one intravenous injection of arsphenamin the reactions obtained, Oct. 11, 1919, were: Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 1 per cubic millimeter; colloidal gold test, 543321000.

Case 5.—*History.*—The patient was a woman, 37 years of age at the time of the first examination, who had a definite clinical picture of tabes dorsalis. For eight years she had been having sharp pains in the legs which had finally become so severe that she had to give up her work. An ataxic gait had developed, the difficulty in walking being most marked when it was dark.

Examination.—Neurologic examination showed unequal, poorly reacting pupils; absence of knee jerks and ankle jerks; ataxia in walking and a Romberg sign. The serology was interesting; a positive blood Wassermann reaction but a negative Wassermann reaction in the spinal fluid were obtained. There was a suggestion of a globulin ring by the Ross-Jones test but hardly enough to be called a definite reaction. There were 139 cells per cubic millimeter and an almost negative colloidal gold reaction, 0011230000.

Course and Treatment.—Under treatment, consisting of the injection of arsphenamin and mercury, she improved rapidly. The pains practically disappeared, and she found walking less difficult. She was enabled to return to work.

After thirty-two injections of arsphenamin and eight of mercury salicylate a second lumbar puncture was performed. The blood Wassermann reaction was negative, but the spinal fluid gave a strongly positive reaction; globulin was present; the cell count was 30 per cubic millimeter, and the colloidal gold test had become strongly positive, 5444310000.

Blood and Spinal Fluid Reactions.—The reactions obtained before treatment, Jan. 23, 1919, were: Wassermann reaction of the blood, positive; Wassermann reaction of the spinal fluid, negative; globulin, ±; albumin, ±; cells, 139 per cubic millimeter; colloidal gold test, 0011230000. After thirty-two injections of arsphenamin and eight injections of mercury the reactions obtained, Oct. 4, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 550000; globulin, +; albumin, +; cells, 30 per cubic millimeter; colloidal gold test, 5444310000.

Case 6.—*History.*—This case shows the provocative reaction in the ventricular fluid after intraventricular injections. The patient was suffering from taboparesis and was quite demented. He had acquired syphilis about nineteen years before, receiving treatment at that time. He had been deteriorating mentally for about two years before appearing at the clinic and had received a few injections of arsphenamin but was rapidly becoming worse. He was given intraventricular injections of arsphenamized serum.

Examination. — Examination at the time of the intraventricular injection showed unequal, irregular pupils which did not react to light but did react to accommodation; the knee jerks and ankle jerks were absent; there was a speech defect. He was depressed, memory was poor, calculating ability nil (he was a civil engineer), and he was irritable and emotionally unstable. The spinal fluid was positive in all tests.

On Dec. 15, 1919, a trephine opening was made in the calvarium by Dr. W. J. Mixter at the Massachusetts General Hospital. Fluid was withdrawn from the lateral ventricle and 15 c.c. of Swift-Ellis serum was injected. A lumbar puncture was performed at the same time. The spinal fluid was strongly positive, whereas the ventricular fluid was negative. A second ventricular fluid examination in February, 1920, was again essentially negative. On April 6, 1920, the ventricular fluid showed a relatively strong colloidal gold reaction, 4431000000; all other reactions were negative. However, on May 4, 1920, all tests had become positive, with the exception of the cell count. During this period from December, 1919, to May, 1920, the patient had received fifteen intravenous injections of arsphenamin, one intraspinal injection of arsphenamized serum and four intraventricular injections of serum, three of which were arsphenamized. The patient showed some clinical improvement.

In this case we would appear to have provoked positive reactions in the ventricular fluid.

Ventricular Fluid Reactions.—The reactions obtained, Dec. 17, 1919, before treatment, were: Wassermann reaction of the ventricular fluid, negative; globulin, 0; albumin, normal; cells, 1 per cubic millimeter; colloidal gold test, negative. After two intraventricular injections of arsphenamized serum and eight intravenous injections of arsphenamin the reactions obtained, Feb. 20, 1920, were: Wassermann reaction of the ventricular fluid, negative; globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, 2100000000. After one intraventricular injection of arsphenamized serum, one intraspinal injection of arsphenamized serum and five intravenous injections of arsphenamin the reactions obtained, April 6, 1920, were: Wassermann reaction of the ventricular fluid, negative; globulin, 0; albumin, normal; cells, 1 per cubic millimeter; colloidal gold test, 4431000000. After one intraventricular injection of arsphenamized serum and two intravenous injections of arsphenamin the reactions obtained, May 4, 1920, were: Wassermann reaction of the ventricular fluid, 522———; globulin, 2; albumin, 2; cells, 1 per cubic millimeter; colloidal gold test, 55553200000.

These cases illustrate the fact that after antisyphilitic treatment a negative spinal fluid may become positive, or one that is slightly positive may give more strongly positive reactions.

In Case 1 the diagnosis was cleared by the effect of a provocative injection of arsphenamin. In this case the spinal fluid, which was negative prior to antisyphilitic treatment, became strongly positive in all tests after one injection of arsphenamin. It is worth while to note that the blood did not become positive. This result is also found in the other cases of this series.

Case 2 of the series shows the intensification of the spinal fluid Wassermann reaction after intravenous injection and also the provocation of a positive colloidal gold reaction, globulin and pleocytosis. It is perhaps of interest to point out in this discussion the curious fact that no provocative change was noted in the serum Wassermann reaction. In the light of present knowledge perhaps one may conclude that the patient is cured so far as visceral involvement is concerned. A latent focus of spirochetes in the nervous system was apparently activated by treatment, as was manifested by the provocative spinal fluid changes. This case is of further interest from the standpoint of conjugal neurosyphilis: paresis in the wife and latent neurosyphilis in the spouse.

The patient in Case 3 presented so definite a picture of tabes that there could be no doubt of the diagnosis, despite a spinal fluid that was negative except for a small amount of globulin and albumin increase. No provocative result occurred either in the blood or spinal fluid as the result of intravenous injection, but intraspinal subdural injections of arsphenamized serum provoked a positive Wassermann and a positive gold reaction. It is worth while to note that under treatment these reactions were reduced to almost normal. From the clinical standpoint, improvement took place even during the period in which the tests became more strongly positive. The patient, confined to bed, in the paralytic state of tabes, became able to walk without a cane, although quite ataxic.

The patient in Case 4 had undoubted tabetic disease, showing negative blood and spinal fluid reactions. Under intraspinal subdural injections the spinal fluid showed positive globulin, albumin, pleocytosis and gold reaction, but the blood and spinal fluid Wassermann tests remained negative. Contrary to the experience in Case 3, no improvement in the patient resulted from this treatment.

Case 5 is that of another patient on whom the clinical evidence made a diagnosis of tabes certain, but whose spinal fluid Wassermann reaction was negative. The blood, however, was positive, and there were 139 cells per cubic millimeter in the fluid. Under intravenous injections of arsphenamin, the Wassermann reaction in the blood serum became negative, while, on the other hand, the spinal fluid Wassermann reaction became positive. The cell count decreased, but the colloidal gold reaction became more strongly positive. From the clinical standpoint, the result of treatment was eminently satisfactory, as all pain disappeared, the ataxia became markedly improved, and the patient was able to return to work, after having been incapacitated for some months prior to treatment.

The patient in Case 6 showed the provocative results in the ventricular fluid after intraventricular injections, similar to those observed in the spinal fluid of the preceding cases.

Altman and Dreyfus[2] have shown that arsphenamin may have a provocative influence on the spinal fluid in cases of primary and secondary syphilis. They examined the spinal fluid in the primary and secondary period of the disease, both before and after the intravenous administration of arsphenamin. One of their cases may be reviewed: A patient who presented no subjective or objective symptoms of nervous involvement and whose spinal fluid was negative, received 0.4 gm. arsphenamin intravenously. He then absented himself from the clinic for a period of seven weeks. When he returned, he presented a facial paralysis and an involvement of the eighth nerve. The spinal fluid at this time showed a high pleocytosis, much globulin and a positive Wassermann reaction in both high and low dilutions of the spinal fluid. The serum Wassermann reaction on both occasions was positive. These writers speak of this phenomenon as a provocative neurorecidive. A criticism of this conclusion might be offered, as it is quite possible that the condition had nothing to do with the introduction of arsphenamin, but might have occurred had it not been injected. As this occurred some time after the injection, and as there was only one injection, this case cannot be considered as strong evidence, but as illustrative of this type of reaction.

A study similar to that of Altman and Dreyfus was made by one of us (J. V. K.).[3] In a series of twenty-five cases of secondary syphilis, the spinal fluid was examined before and after a course of four intravenous injections of arsphenamin, administered at intervals of seven to ten days. Provocative spinal fluid changes were observed in some of the cases on the second examination of the spinal fluid. This observation, and those of Altman and Dreyfus are in accord with the hypothesis of Gennerich,[4] that arsphenamin is capable of provocative spinal fluid changes in the early period of syphilis.

The provoking of a spinal fluid by arsphenamin therapy from negative to positive is, in all probability, the expression of a Herxheimer reaction. A neurorecidive or neurorecurrence following arsphenamin injection is probably a clinical expression of this reaction. The apparent provocative reactions in the spinal fluid of neurosyphilitic patients, as herein reported, would seem to be of a similar nature and in line with the statements made above.

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[2] Altman and Dreyfus: München. med. Wchnschr. **60**:464; 531, 1913.

[3] Klauder, J. V.: Am. J. Syphilis **3**:559 (Oct.) 1919.

[4] Gennerich: Die Liquorveränderungen in den einzelnen Studien der Syphilis, Berlin, 1913.

PROVOCATIVE REACTION NOT FREQUENT

It should be emphasized that this provocative reaction is not a frequent occurrence even in cases in which there is evidence of central nervous system involvement with negative findings in the spinal fluid. This may be illustrated by the following cases:

Case 7.—The patient, a man aged 36, came to the hospital after an attack of pneumonia, complaining of feeling weak. Examination showed Argyll Robertson pupils and active knee reflexes. The Wassermann reaction was positive in the blood. The spinal fluid reactions were negative. A colloidal gold test was not made at this time. The patient was given antisyphilitic treatment, which was continued for over a year. Four consecutive negative Wassermann reactions of the blood serum were then obtained. A lumbar puncture at this time was again entirely negative, except for the colloidal gold reaction, which gave a paretic type of curve, 5553000000.

Case 8.—A man, aged 35, who was brought to the hospital because of hallucinations and delusions which were apparently the result of alcoholic indulgence, had acquired syphilis a year before, for which he had been treated, and had been discharged with a negative Wassermann reaction of the blood. On admission to the hospital for his hallucinosis, he gave a negative blood Wassermann reaction and a negative spinal fluid Wassermann reaction but a pleocytosis, excess of globulin and albumin, and a paretic gold reaction. Several intravenous injections of arsphenamin were given for provocative effect, but none was found either in the blood or spinal fluid.

There appears to be some evidence that certain cases of neurosyphilis are made worse by arsphenamin therapy. This matter, which is discussed in numerous places under the heading of neurorecidive or neurorecurrence, has had proponents and opponents in great numbers. It seems to us, however, that there is considerable clinical evidence that occasional cases of neurorecurrence are caused by arsphenamin injection. This is much more frequent, probably, in the secondary period of the disease than later. The reactions to arsphenamin doubtless manifest the powerful spirocheticidal action of the drug. The arsphenamin either activates foci of spirochetes or, as a result of the lysis of great masses of organisms, the toxins are liberated in large amounts, which produces pathologic results. We may then, assume that this result is expressed in a laboratory way by the appearance of provocative reactions in the blood and spinal fluid, and in a clinical way by the appearance of neurorecidives and the accentuation of symptoms.

UNFAVORABLE RESULTS OF THERAPY

The two following cases may be given as illustrations of unfavorable results of therapy:

Case 9.—The patient was a boy, aged 9 years, with the evidence of congenital syphilis. There were three miscarriages preceding his birth. At an early age he developed snuffles and had a skin rash. The family doctor made a diagnosis of blood disease, and he was given inunctions of mercury. At the age of 6 he had eye trouble, which was diagnosed as interstitial keratitis. He was given four injections of the diarsenol brand of arsphenamin, 0.15 gm. each, in a period of six weeks. He was then given mercury by mouth. About two weeks after the discontinuance of the arsphenamin, he sustained a left sided paralysis.

Case 10.—A man, 49 years of age, gave a history of a genital lesion thirty-two years previously. Twenty-five years after the lesion appeared, he began to suffer with acute attacks of indigestion. At that time the onset of his present symptoms began. When seen seven years after the onset of symptoms he was having gastric crises, lancinating pains, sphincter disturbances, girdle sensation, impotence, diplopia and impaired memory. He was given two injections of neo-arsphenamin, 0.9 gm., with a week between the injections. He experienced a severe reaction each time. He was confined to bed for two days after the first injection and for four weeks after the second. He was said to be out of his mind. The pains in his legs became more severe and his speech was affected. A year later he showed some improvement.

While many such cases could be reported, they are not usual, but represent a small minority of all cases. Our purpose in calling attention to them at this time is for comparison with the provocative results shown in the spinal fluid examination of the first five cases of this series.

SPINAL FLUID FINDINGS AS AN INDICATION FOR TREATMENT

Our intention is not to discuss the indications or contraindications for treatment of syphilis or neurosyphilis, but rather to present in concrete form the type of Herxheimer reaction represented by changes in the spinal fluid. Nevertheless, a word may be said concerning the bearing of these findings on the question of treatment. From this standpoint, probably the most important group is that containing cases that may be considered as latent neurosyphilis, that is, cases in which, although there is evidence of syphilitic activity in the nervous system as shown by the spinal fluid findings, the patient is without symptoms. In some instances, as in the second case of our series, the spinal fluid finding may be mild, such as a positive Wassermann reaction only. Was harm done in this case because the reactions became stronger after treatment? It might be stated that a continuation of treatment produced a diminution in these findings; in Cases 3 and 5, good results are to be accredited to treatment, despite the intensification of the spinal fluid findings. In Cases 3 and 5 the treatment was of great value as the patients were in better condition than they were before treatment. Possibly some difference of opinion as to the value of treating patients with latent neurosyphilis will depend on a theoretical difference of opinion. Thus, there is a school of syphilologists who believe that syphilis is an incurable disease and that all that therapy can be expected to accomplish is the production of a latent condition. Another group, that may be considered as somewhat more optimistic, believes that syphilis is a curable condition, and that a great effort should be made to produce negative serology. It is quite obvious, of course, that both conceptions may be carried to a degree that is not rational. The neurologist will usually hold that the only way to prevent the occurrence of the symptoms of neurosyphilis is to treat the patients intensively before these symptoms have occurred, and it is generally held that the appearance of pathologic findings in the spinal fluid is a certain forerunner of destructive lesions. On the other hand, it would appear advisable to discontinue treatment in cases that are apparently quiescent for years and in which treatment seems to have little effect on the spinal fluid findings and which do not show any clinical improvement.

We should like to make clear, in conclusion, that these provocative changes and the cases in which, from the clinical standpoint, the condition becomes worse after treatment, are, in reality, few in number and not of sufficient frequency to cause concern.

SUMMARY

Case histories are given to show that after treatment the cerebrospinal fluid, which was negative before treatment, may become positive in all routine tests, or a weakly reacting fluid may become much stronger. This is called a provocative reaction. It may be accomplished by the intravenous or intraspinal injection of arsphenamin. This is compared to the Herxheimer reaction or the production of neurorecurrences and is considered as the laboratory analogue. The provocative reactions are shown to occur in both the ventricular and spinal fluids. This is not a frequent phenomenon, and patients with vascular neurosyphilis with negative cerebrospinal fluids may not react in this manner. However, diagnosis may occasionally be made clear in obscure cases. In none of the cases in this series was the provocative reaction obtained with the blood serum. Despite the increase in the strength of the spinal fluid reactions, clinical improvement may result, and continued treatment may again produce a negative fluid.

A CLINICAL STUDY OF THE REACTIONS FOLLOWING THE INTRAVENOUS ADMINISTRATION OF ARSPHENAMIN IN NONSYPHILITIC PERSONS *

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Ten years have now elapsed since arsphenamin (salvarsan) was first introduced by Paul Erlich and his associates, and during that space of time many thousands of doses of this remedy have been administered. Almost from the beginning and extending to the present, untoward symptoms have been noted following the intravenous administration of arsphenamin. Many hypotheses have been advanced to explain these reactions, but as yet no method has been suggested which would eliminate these untoward reactions.

In this study, arsphenamin (Dermatological Research Laboratory) of the same serial number was administered to both syphilitic and nonsyphilitic patients, and the reactions following their intravenous administration were noted. It was believed that a study of this nature might throw some light on the possible cause or causes of these untoward symptoms.

SYMPTOMS IN SYPHILITIC AND NONSYPHILITIC PATIENTS

The reactions following the intravenous administration of arsphenamin are classified into: (1) immediate, (2) early, and (3) late symptoms. We shall concern ourselves in this discussion with a study of the early symptoms which were noted following the intravenous administration of arsphenamin to the nonsyphilitics and compare them with the symptoms observed when the identical product was administered to syphilitic patients.

The symptoms observed in the nonsyphilitic series were headache, chills, fever, nausea, vomiting, diarrhea, and backache. Two patients

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of this series developed cutaneous manifestations; one of the eruptions was scarlatinoid in character, and the other presented the characteristics of a vesicular eczema. Both patients made uneventful recoveries.

In all, 114 injections were administered to nonsyphilitic patients. Table 1 details the results obtained in our syphilitic series.

TABLE 1.—Reactions to Arsphenamin in Normal Persons

Case	Lot	Dose	Reaction
1	3586	0.5	No reaction
2	2586	0.5	Fever, chills, headache, nausea, vomiting, pains in stomach
3	3586	0.5	No reaction
4	3586	0.5	Chills, nausea, loose bowels, no appetite
5	3586	0.5	Chills, fever
6	3586	0.5	Slight fever and loose bowels
7	3586	0.5	Slight nausea
8	3586	0.5	Chills and headache
9	3586	0.5	Headache, nausea, loose bowels, backache
10	3586	0.5	Slight chills and headache, nausea, loose bowels
11	3586	0.5	No reaction
12	3586	0.5	Chills, headache, nausea, loose bowels, no appetite
13	3586	0.5	Headache
14	3586	0.5	Fever, chills, headache, nausea, loose bowels
15	3586	0.5	Fever, chills, headache, nausea
16	3586	0.5	No reaction
17	3540	0.45	Fever, chills, headache
18	3540	0.45	Fever, chills, headache, nausea, loose bowels
19	3546	0.5	Chills, headache, nausea, vomiting, loose bowels, no appetite
20	3546	0.5	No reaction
21	3546	0.5	Headache, nausea, loose bowels
22	3546	0.5	Chills, headache, nausea, loose bowels
23	3546	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
24	3546	0.5	Nausea, loose bowels
25	3546	0.5	Nausea
26	3855	0.5	Fever, chills, headache, nausea, loose bowels, aching of kidneys
27	3855	0.5	Fever, headache, nausea, vomiting at hospital, loose bowels
28	3855	0.5	No reaction
29	3855	0.5	No reaction
30	3843	0.5	Chills, headache, nausea, loose bowels, dizzy
31	3843	0.5	Fever, headache, loose bowels
32	3843	0.5	Nausea, vomiting, sleepy
33	3829	0.5	No reaction
34	3829	0.5	No reaction
35	3829	0.5	No reaction
36	3829	0.5	No reaction
37	3829	0.5	Nausea
38	3829	0.5	Fever, headache
39	3829	0.5	Headache, nausea
40	3829	0.5	Fever, nausea
41	3829	0.5	Chills (little)
42	3829	0.5	Headache (slight)
43	3829	0.5	Slight fever and headache
44	3829	0.5	Nausea
45	3829	0.5	Chills, nausea, vomiting
46	3829	0.5	No reaction
47	3829	0.5	Fever, chills, nausea, loose bowels
48	3829	0.5	Headache, vomiting, loose bowels, backache
49	3829	0.5	Nausea
50	3829	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
51	3829	0.5	No reaction
52	3829	0.5	No reaction
53	3829	0.5	No reaction
54	3829	0.5	Slight nausea, backache
55	3829	0.5	No reaction
56	3829	0.5	Fever, headache, vomiting, loose bowels
57	3829	0.5	No reaction
58	3829	0.5	Chills, headache
59	3829	0.5	No reaction
60	3829	0.5	No reaction
61	3829	0.5	Headache, nausea, loose bowels
62	3884	0.5	Fever, chills, nausea, loose bowels
63	3884	0.5	Chills, nausea and loose bowels
64	3884	0.5	No reaction
65	3895	0.6	Loose bowels
66	3895	0.6	No reaction

TABLE 1.—Reactions to Arsphenamin in Normal Persons—(*Continued*)

Case	Lot	Dose	Reaction
67	3900	0.5	Headache
68	3900	0.5	Headache, nausea, vomiting, loose bowels
69	3878	0.6	Fever, chills, headache, nausea, vomiting, loose bowels
70	3903	0.6	Chills, loose bowels
71	3903	0.6	Nausea, loose bowels
72	3895	0.5	Chills, headache, nausea, loose bowels
73	3895	0.5	Headache
74	3895	0.5	Headache, nausea, vomiting, loose bowels, backache
75	3895	0.6	Fever, chills, headache, nausea, vomiting
76	3895	0.5	No reaction
77	3895	0.6	Fever, chills, headache, nausea, loose bowels, weak and nervous
78	3895	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
79	3900	0.5	Headache, nausea, loose bowels, pain in shoulder blade
80	3900	0.5	Chills
81	3900	0.5	Headache
82	3900	0.5	Headache, nausea, vomiting, loose bowels
83	3900	0.5	Chills, nausea
84	3900	0.5	No reaction
85	3900	0.5	Vomiting, constipation
86	3900	0.5	No reaction (drowsy)
87	3900	0.5	Headache, nausea
88	3900	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
89	3900	0.5	Headache
90	3900	0.5	Loose bowels
91	3928	0.45	No reaction
92	3928	0.45	No reaction
93	3937	0.6	No reaction
94	3928	0.6	Headache, loose bowels
95	3903	0.5	Headache, nausea, loose bowels
96	3903	0.5	No reaction
97	3903	0.5	Loose bowels
98	3903	0.5	No reaction
99	3903	0.5	No reaction
100	3903	0.5	Nausea, vomiting, loose bowels
101	3903	0.5	No reaction
102	3903	0.5	Fever, headache and loose bowels
103	3903	0.5	No reaction
104	3937	0.5	Nausea, loose bowels
105	3937	0.5	Loose bowels
106	3937	0.5	No reaction
107	3937	0.5	Fever
108	3937	0.5	No reaction
109	3937	0.5	Headache
110	3937	0.5	Loose bowels
111	3937	0.5	Loose bowels
112	3937	0.4	Loose bowels (slightly)
113	3937	0.5	No reaction
114	3855	0.5	Loose bowels

Of this number seventy-seven, or 67 per cent., gave evidence of some reactive symptoms. Twenty-five, or 32 per cent., complained of fever; thirty-one, or 40 per cent., of chills or chilliness; forty-six, or 60 per cent., of headache; forty-seven, or 60 per cent., of nausea; eighteen, or 23 per cent., of vomiting; forty-six, or 60 per cent., of diarrhea, and five, or 6 per cent., of backache.

Table 2 gives in detail the reactions reported by the syphilitic patients, receiving the arsphenamin of the same serial numbers as the nonsyphilitic patients. The symptoms complained of were identical in both classes of subjects.

In all, the records of the reactions of ninety-three syphilitics were tabulated. Of this number, sixty-two, or 66⅔ per cent., reported some evidence of reaction. Twenty-five, or 40 per cent., complained of fever; twenty-six, or 42 per cent., of chills and chilliness; thirty-seven, or 60 per cent., of headache; thirty-seven, or 60 per cent., of nausea; twenty-six, or 40 per cent., of diarrhea; eleven, or 18 per cent., of vomiting and four of backache.

TABLE 2.—Reactions to Arsphenamin in Syphilitic Persons

Case	Lot	Dose	Reaction
1	3586	0.5	No reaction
2	3586	0.5	Fever, chills, headache, nausea, loose bowels, pains in body
3	3586	0.5	No reaction
4	3540	0.5	No reaction
5	3540	0.5	No appetite
6	3540	0.5	No reaction
7	3540	0.5	Slight chills, nausea and loose bowels
8	3546	0.5	Headache, heart and body hurts her
9	3546	0.5	Headache
10	3547	0.5	No reaction
11	3546	0.5	Chills, nausea, loose bowels, heart-burn
12	3855	0.5	No reaction
13	3855	0.5	No reaction
14	3855	0.5	Chills, headache, body hurts and face is swollen
15	3855	0.5	Fever, chills, headache, nausea, loose bowels, pains through body
16	3855	0.5	Fever, headache, stiff joints
17	3855	0.5	Vomiting, tired feeling in back, also slight pains
18	3855	0.5	Fever, chills, nausea, loose bowels, nervous
19	3855	0.5	Chills, headache, nausea, pains in legs
20	3843	0.5	Fever, chills, headache
21	3843	0.5	Headache, loose bowels, feet hurt
22	3843	0.5	Fever, headache, stiff joints
23	3843	0.5	No reaction
24	3843	0.5	Nausea, nervousness
25	3829	0.45	No reaction
26	3829	0.45	Fever, headache, constipated, stiff joints
27	3829	0.5	Headache
28	3829	0.45	No reaction
29	3829	0.45	Chills, headache, nausea, vomiting
30	3829	0.45	Nausea, itching on calf and shins
31	3829	0.45	No reaction
32	3829	0.5	Headache, nausea, vomiting
33	3829	0.45	Fever, chills, headache, loose bowels
34	3829	0.5	Chills, nausea, vomiting, loose bowels
35	3829	0.45	Fever, chills, headache, nausea, loose bowels, pains in body
36	3829	0.5	No reaction
37	3829	0.45	No reaction
38	3829	0.5	No reaction
39	3829	0.5	Chills, headache, nausea, pains in legs
40	3829	0.5	Fever
41	3829	0.5	Fever, chills, nausea and loose bowels
42	3829	0.5	Headache, nausea, loose bowels
43	3829	0.5	Loose bowels
44	3829	0.5	Vomiting, dull feeling in head, tired limbs
45	3884	0.5	Headache, nausea, vomiting
46	3884	0.5	Headache, nausea, loose bowels
47	3884	0.5	Fever, chills, headache, loose bowels
48	3884	0.5	Chills, headache, nausea, loose bowels
49	3884	0.5	Nostril trouble
50	3895	0.45	Fever, headache, nausea
51	3895	0.45	Nausea, loose bowels
52	2895	0.45	Nausea, vomiting, loose bowels, tired in limbs
53	3900	0.45	Headache
54	3900	0.45	No reaction
55	3900	0.45	No reaction
56	3878	0.3	No reaction
57	3878	0.3	Chills, headache
58	3903	0.4	No reaction
59	3903	0.4	Fever, headache, nausea, weakness, pains in knees
60	3895	0.5	Fever, chills, headache, nausea
61	3895	0.5	(Spitting)
62	3895	0.5	Fever, headache, joints ache
63	3895	0.4	Fever, headache, nausea, loose bowels
64	3895	0.5	No reaction
65	3895	0.45	No reaction
66	3895	0.4	Vomiting, loose bowels, tired feeling in limbs
67	3895	0.5	No reaction
68	3895	0.5	No reaction

TABLE 2.—Reactions to Arsphenamin in Syphilitic Persons—(*Continued*)

Case	Lot	Dose	Reaction
69	3895	0.5	Fever, chills, headache, nausea, loose bowels (arm swollen and sore)
70	3895	0.4	Headache, nausea, loose bowels
71	3895	0.5	Chills, nausea, pains in back
72	3895	0.4	Fever, chills, headache, nausea, vomiting
73	3895	0.5	Pains over eyes
74	3900	0.5	Fever, chills, headache, nausea, loose bowels
75	3900	0.5	Nausea, pains in chest and shoulders
76	3900	0.5	Fever, headache, nausea, loose bowels
77	3900	0.5	Fever, chills, nausea
78	3900	0.5	No reaction
79	3928	...	Chills, headache
80	3928	0.4	No reaction
81	3928	...	No reaction
82	3937	0.4	Nausea, vomiting
83	3937	0.4	Loose bowels
84	3937	0.4	No reaction
85	3928	0.4	Fever, chills, headache, nausea, vomiting, pains in the legs
86	3928	0.4	Nausea
87	3928	0.4	Weak
88	3903	0.45	Nausea
89	3903	0.45	Fever, chills, headache, loose bowels
90	3903	0.45	Feels tired
91	3903	0.45	Headache, nausea, loose bowels
92	3937	0.45	No reaction
93	3937	0.45	No reaction

It is to be noted from the study of these tables that the percentage of reactions was equal in both the syphilitic and nonsyphilitic series. The statistical analysis of the tables recorded shows these results:

Fever as a symptom was recorded in 40 per cent. of the syphilitic patients and in 32 per cent. of the nonsyphilitics; diarrhea in 60 per cent. of the nonsyphilitics and in 40 per cent. of the syphilitics; chills in 40 per cent. of the nonsyphilitics and in 42 per cent. of the syphilitics; vomiting in 23 per cent. of the nonsyphilitics and in 18 per cent. of the syphilitics, and headache and nausea occurred in 60 per cent. of both the syphilitic and nonsyphilitic patients.

It will be noted that the percentages of the reactive symptoms registered approach one another so closely in the syphilitic and nonsyphilitic series that no definite conclusions can be drawn from the figures per se.

CAUSES OF REACTIONS

The causes of the reactions following the intravenous administration of arsphenamin can be classified into: (1) factors relative to the patient; (2) factors relative to the technic, and (3) factors relative to the chemical compound employed.

1. *Factors Relative to the Patient.*—There can be but little doubt that the mental state of a patient at the time of treatment influences the occurrences of reactive symptoms. Not only is this true of the intravenous injections of arsphenamin but also of mercurial preparations and other medicinal substances which at times are administered intravenously.

One of us (A. Strickler) gave a series of intravenous mercurial injections to a group of syphilitic patients that had received a large number of arsphenamin treatments. A percentage of these patients that had received these mercurial injections reported some of the reactive symptoms, such as headache, nausea, and chilliness which occur after injections of arsphenamin. Similar reactive symptoms were also reported by patients suffering from nonsyphilitic dermatologic affections who had received intravenous injections of mercurial preparations.

2. *Factors Relative to the Technic.*—Under this caption belongs the discussion of the water error of Wechselmann. Wechselmann believed that water impurities, chiefly bacterial proteins, were largely responsible for febrile and gastro-intestinal reactions. Gennerich believed that organic contamination of water by saprophytes was the cause of a certain number of unfortunate consequences.

In 1910, Neisser advanced the view that the febrile symptoms were due to the rapid destruction of innumerable spirochetes and the setting free of endotoxins which reached the blood stream and induced the symptoms. E. H. Martin, in a discussion of the treatment of syphilis, believed that the temperature and bowel symptoms were due to the endotoxins liberated from killed spirochetes, and nausea and vomiting caused by idiosyncrasy.

Our clinical investigation seems to disprove the views of Neisser. Our records show definitely that the reactive symptoms were just as numerous among the nonsyphilitics that had received intravenous injections of arsphenamin, as among the syphilitic patients that received the same medicament of the same serial number. Our evidence seems to point to the fact that the so-called "syphilitic state" of the patient plays either no rôle or a very minor rôle in the causation of reactive phenomena. There are other faults in technic which at times may be responsible for some reactive symptoms, such as the temperature of the water employed, acidity or excessive alkalinity of the solution, too rapid infusion of the solution and the preliminary preparation of the patient.

3. *Factors Relative to the Medicament.*—We are of the impression that the most important factors in the causation of the reactions following the intravenous injections of arsphenamin are to be found: (*a*) in impurities in the drug, and (*b*) in the chemical reactions which probably take place between the arsphenamin and the chemical constituents of the blood.

Arsphenamin is an extremely complex substance, and before its final elaboration numerous intermediate products must be prepared. Arsphenamin cannot be regarded as an absolutely pure compound because it cannot be purified by repeated crystallization. Arsphenamin does not give arsenic values quite up to the theoretical amount, and furthermore, there are elements present which have no place in the chemical formula. Analyses have shown that arsphenamin contains on the average from 1 to 2 per cent. of sulphur. In view of these statements, it is entirely possible that a medicinal substance, which requires numerous steps for its preparation before its final elaboration, and which is of such complexity, should be capable of producing untoward symptoms when introduced into the blood stream.

SUMMARY

1. Both syphilitic and nonsyphilitic patients may experience similar reactions following the intravenous injections of arsphenamin.

2. The endotoxins, produced presumably by the rapid killing of spirochetes in the blood stream of syphilitic patients, play either no rôle or a very unimportant one in the causation of reactive symptoms.

3. The percentage of reactive symptoms following intravenous injections of arsphenamin is equal in both syphilitic and nonsyphilitic patients.

4. It is our impression that the two most important factors in the production of arsphenamin reactions are (1) the patient and (2) the medicament.

5. Of these two factors, the medicament is far more potent in causing reactive symptoms; the untoward phenomena may be produced either by some impurity in the arsphenamin or by some chemical reaction between the arsphenamin and the chemical constituents of the blood, or both factors may be operative at the same time.

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EFFECTS OF ARSPHENAMIN ON RENAL FUNCTION IN SYPHILITIC PATIENTS *

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CHARLOTTE, N. C.

A short time after arsphenamin came into prominence, renal impairment following its administration was noted in a small percentage of cases. During the first year of its use, Ehrlich[1] called attention to the fact that it should be given judiciously to patients suffering from nephropathies other than syphilitic nephritis. In 1911,[2] Mohr reported three cases of serious renal complications following its use. Two years later, Schlasberg[3] reported twenty-seven cases in all of which albumin and casts developed in the urine. This he attributed to the drug. In order to prove his contention, he injected a number of rabbits and produced in them an experimental nephritis. Other cases have been reported by Geronne, Jadassohn, Scholtz,[4] Wechselmann[5] and others. Wechselmann called particular attention to the deleterious effects on pregnant women and advised Schlayer's lactose test as a precautionary measure in all such cases before administering treatments.

No doubt the drug is more perfect today than it was at that time, and therefore it is less toxic. Perhaps the technic employed then may have been a contributing factor. With our present-day technic and with the perfection of the drug, there are still some patients who develop nephritis after the administration of arsphenamin. The number of such cases cannot be ascertained from the meager literature on the subject. Their occurrence, however, is frequent enough to warrant periodic urine examinations in every patient receiving arsphenamin. As stated by Schlasberg, the microscopic examination should not be omitted since albumin may or may not be present, whereas any marked damage will be detected by the appearance of casts in the sediment. Guy[6] has recently reported observations on 3,000 soldiers who received

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* From the Crowell Urological Clinic.

[1] Ehrlich, quoted by Mohr, R.: Med. Klin. **7**:596, 1911.

[2] Mohr, R.: Med. Klin. **7**:613, 1911; abstr. J. A. M. A. **56**:1517 (May 20) 1911.

[3] Schlasberg: Nord. med. Ark. **45**:1844, 1913; abstr. J. A. M. A. **61**:910 (Sept. 13) 1913.

[4] Quoted by Mohr (Footnote 2).

[5] Wechselmann, W.: München. med. Wchnschr. **51**: 1845 (Aug. 25) 1914; abstr. J. A. M. A. **63**:1431 (Oct. 17) 1914.

[6] Guy, W. H.: Reactions Following the Administration of Arsphenamin: Report of Reaction in a Series of Twenty-Five Thousand Injections, J. A. M. A. **73**:901 (Sept. 20) 1919.

25,000 arsphenamin injections. He saw one death from nephritis, and thirty patients developed transient albuminuria, three of whom had numerous red blood cells and large granular casts in the urine. All of these cases developed after treatments had been administered on a day when all patients reacted. He does not attribute this to the drug but to impurities contained in the water. He draws his conclusions from the fact that he was able to use a drug of the same serial number on other occasions without reactions. Stokes and Busman[7] offer the explanation that the group of reactions reported by Guy might have been due to the rubber tubing. Their cases simulated those described by Guy with the exception that they did not observe any signs of renal complications.

It cannot be denied that in a certain percentage of cases there is some renal damage produced by arsphenamin as shown by Pearce and Brown.[8] Whether these cases of nephritis are caused by arsphenamin or whether they are latent and are only lighted up by the drug, are questions of mere speculation. In order to determine whether all patients might not show some renal functional disturbances following arsphenamin treatments, we picked a number of young men whose average age was 25 years and who so far as we were able to determine had no renal disturbance whatever before treatments were instituted.

TESTS AND RESULTS

As indicators of the influence that arsphenamin might have on renal function, determinations were made of the urea content of the blood by the Van Slyke and Cullen[9] modification of Marshall's urease method and of phenolsulphonephthalein excretion by way of the kidneys by means of the method of Rountree and Geraghty.[10] It was believed that these two tests performed both before and after treatment, together with a careful urinalysis made at the same time, would point out any definite alteration in renal function if such were produced. All tests in order to be comparable were performed by the same method in detail, under the same circumstances as far as possible, and read by the same observer. The phenolsulphonephthalein was administered by the intramuscular route. The initial function test was made the day before or on the day of the first treatment; the final test was made the day following the last injection of the course.

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[7] Stokes, J. H., and Busman, G. J.: Tubing as a Cause of Reaction to Intravenous Injection, Especially of Arsphenamin: Preliminary Report, J. A. M. A. **74**:1013 (April 10) 1920.

[8] Pearce, Louise, and Brown, W. H.: J. Exper. M. **22**:517, 1915.

[9] Van Slyke and Cullen: J. Biol. Chem. **19**:211, 1914.

[10] Rountree, L. G., and Geraghty, T. J.: J. Pharmacol. and Exper. Therap. **2**:579, 1910.

For obvious reasons four nephritics with syphilis coming under observation at this time were not included in the group. The case of one of these patients will be reported separately as a case of acute syphilitic nephritis; another was a case of chronic nephritis in a man past middle age; and the other two were in young men who were discovered to have a definite nephritis after having had some treatment and who may have had a pre-existing nephropathy. Owing to the fact that our patients were not hospitalized it was difficult to obtain complete data on all cases and therefore a portion of our work had to be discarded.

In twenty patients on whom phenolsulphonephthalein determinations were made both before and after a course of six arsphenamin injections with a total dosage of 2.7 gm., the average phenolsulphonephthalein excretion before treatment was 51.9 per cent. for two hours as compared with 47.7 per cent. excretion after completing treatment. Five, or 25 per cent., showed a reduction of from 10 to 17 per cent. each, while the other fifteen, or 75 per cent., remained the same at both determinations or showed only a slight reduction after treatment. Only one patient showed a higher phenolsulphonephthalein excretion. The urea content of the blood in twenty cases showed an average of 30.7 mg. per 100 c.c. before treatment, and 34.4 mg. after treatment, while one showed an increase of 19 mg. Four cases, or 20 per cent., remained the same, while three, or 15 per cent., showed a decrease of 1 to 3 mg. each. On the whole the changes in 75 per cent. were not significant.

In forty-four cases in which only the first phenolsulphonephthalein was secured the average excretion for two hours was 53.1 per cent.—closely comparable to the 51.9 per cent. in the twenty cases mentioned. In twenty-eight cases in which the phenolsulphonephthalein test was not performed until the treatment was completed, the average excretion was 49 per cent., closely resembling the final phenolsulphonephthalein excretion of 47.7 per cent. in the group previously mentioned.

The question as to whether those patients receiving two arsphenamin injections a week would show a definite variation from the results obtained with the patient receiving injections at weekly intervals, led us to separate a group of patients treated twice a week with the same total dosage. The results in this group were outlined in the accompanying table.

It is noteworthy that the resulting figures in this table do not vary greatly from those obtained in the cases less intensively treated. These nine patients showed an average phenolsulphonephthalein excretion treatment of 50.4 per cent. and an excretion of 44 per cent. after treatment. The blood urea figures are 33.7 mg. and 35.3 mg., respectively. Three, or 33⅓ per cent. of the cases showed a phenolsulphonephthalein reduction of from 10 to 17 per cent. each, although there was no other clinical or laboratory evidence of impaired renal function. The blood ureas showed very little change, but there was a tendency to be higher after treatment.

Results in a Group of Patients Treated Twice a Week

Patient	Age	Diagnosis Syphilis	Wassermann Reaction	Phenolsulphonephthalein Excretion		Blood Urea	
				Before	After	Before	After
1. P. B. S.	27	Primary	++++	$\frac{42 - 10}{52}$	$\frac{29 - 12}{41}$	32	36
2. Sch.	31	Primary	++++	$\frac{33 - 18}{51}$	$\frac{38 - 12}{50}$	36	40
3. E. L. C.	50	Primary	Negative	$\frac{27 - 20}{47}$	$\frac{25 - 17}{42}$	36	34
4. W. W. B.	25	Secondary	++++	$\frac{25 - 16}{41}$	$\frac{15 - 25}{40}$	32	37
5. H. H.	20	Primary	Negative; dark-field, positive	$\frac{31 - 16}{47}$	$\frac{22 - 10}{32}$	27	31
6. J. Q. H.	16	Primary	Negative; dark-field, positive	$\frac{38 - 20}{58}$	$\frac{29 - 12}{41}$	32	31.2
7. B. F. R.	30	Tertiary	++++	$\frac{34 - 17}{51}$	$\frac{37 - 14}{51}$	34	37.2
8. P. T.	24	Primary	++++	$\frac{34 - 19}{53}$	$\frac{23 - 25}{48}$	43	43
9. W. S.	40	Primary	++++	$\frac{39 - 15}{54}$	$\frac{34 - 16}{50}$	31.2	28.2
Average 9 cases				50.4	44	33.7	35.3

The patient with acute syphilitic nephritis, previously mentioned, who was under observation at this time, showed an initial high blood urea reading which rapidly declined under arsphenamin treatment, illustrating presumably the beneficial effect of arsphenamin on this type of nephritis. On the other hand, the phenolsulphonephthalein excretion, which was rather high to begin with, declined somewhat during the treatment in spite of the obvious renal improvement as evidenced by the decline in the blood urea content and the disappearance of the albumin. These findings suggest that the admitted inadequacy of the phenolsulphonephthalein test to detect acute nephritides applies also to syphilitic nephritis.

Recently, we have supplemented the other test with blood creatinin determinations. Since we do not have parallel determinations with this test, our results so far do not permit of comparisons and the report of our findings must be withheld until a later date.

PENICILLIUM BREVICAULE VAR. HOMINIS SACCARDO, 1877, BRUMPT AND LANGERON, 1910, IN AN AMERICAN CASE OF RINGWORM OF THE TOES *

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In 1910 Brumpt and Langeron [1] recorded two cases of ringworm of the toe-nails from which they obtained the species of coco-brown fungus above indicated. Last year (1919) Wile and Gaudin [2] made a very brief report of thirteen cases of onychomycosis, seven of which furnished *P. brevicaule*. These are the only cases I have been able to locate in the literature in which this organism is concerned, and I believe therefore that it is the first time it has been reported in an American.

BRUMPT AND LANGERON'S CASES

The disease had been present for ten years on the right great toe of a man, aged 32 years. It had also existed on the right second toe of his mother, aged 68, for fifteen or twenty years. In extemporaneous potash preparations Brumpt and Langeron found mycelia, chlamydospores and conidia; they stated that the filaments recalled those of Madurella and Indiella.

They cultivated the organism pure (except for staphylococci) on each of five trials. It grew easily on usual mold medium at room temperature, became coco-brown, and under the microscope showed the penicillium type of sporangia, brown lemon-shaped or spherical conidia (spores) and vesicles on the mycelia. Brumpt and Langeron's text-book description is naturally short, but it implies that they made a deeper study which appears to deserve a more detailed report, but if this was ever made, I have been unable to locate it. I can confirm all their observations; which are easily sufficient, taken with their illustrations of the fungus, to satisfy any one that the organism I have cultivated is the same as theirs. They conclude by saying that this is the first penicillium to be observed in a lesion and subsequently cultivated in the hanging drop. This indicates how unusual it is to cultivate this ubiquitous genus (penicillium) of fungi when pathogenic, even though it has been observed in several (for the most part tropical) diseases (Figs. 1 and 2).

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* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

1. Brumpt and Langeron: Precis de Parasitologie, Paris, Masson et Cie, 1910, p. 838.

2. Weil, P. E., and Gaudin, C.: Compt. rend. Soc. de biol. **82**: 121, 1919.

WEIL AND GAUDIN'S CASES

These authors reported thirteen cases out of some hundreds of patients examined. They stated that the species of fungus at fault could not be predicated from clinical appearances, and that the hypertrophic form of onychomycosis could proceed to the grade of onychogryphosis. From the laboratory side they stated that (unlike Brumpt and Langeron) they obtained many kinds of molds in cultures. They gave no details of methods, only the cultural results. These were: *P. brevicaule*, six cases; *Scopulariopsis* (sp.?), one case; *Spicaria* (sp.?), four cases (associated in one with *P. brevicaule*); *Sterigmatocystis*, five cases.

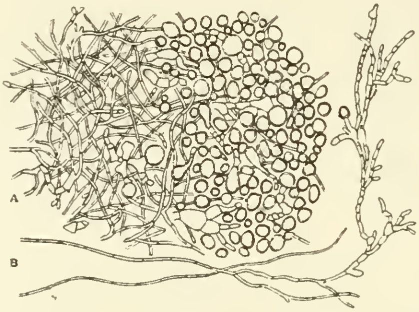

Fig. 1.—Reproduction from Brumpt. Appearance of the fungus in scrapings. A, from first case; B, from second.

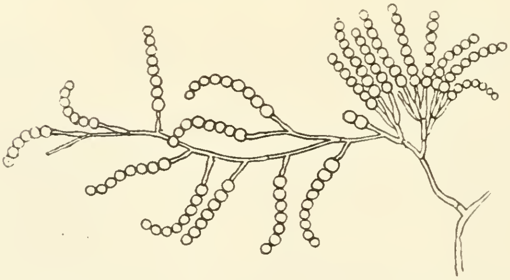

Fig. 2.—Reproduction from Brumpt. Schema of the fungus in culture.

AUTHOR'S CASE

History.—W. H. K., a white man, aged 64, a shoemaker, invalided by chronic valvular cardiac disease, in addition to cardiac symptoms had developed in the past two months a persistent, furiously itching, dry scaly eczema around the waist, which I ascribed to digitalis medication. Scrapings from these positions showed no fungi.

The condition on his toes had endured over thirty years and had never given him any trouble. He stated that from time to time the great toe nails had dropped off and slowly regrown. He recalled no injuries to these parts.

Examination.—On examination it was found that all of his nails lacked the normal luster, but that only three of them were diseased. Both great nails were thickened and lusterless. Their free edges were underlaid by crumbly keratin, and the upper surface was uneven as though from erosion. Flakes and lamellae of keratin on the surface had a pale, coco-brown color. The second toe of the left foot was also opaque and thickened, but in other respects differed materially from the others. It was black, the surface was smooth and the whole nail so loose that only a little force was necessary to remove it bodily from its matrix (Fig. 3).

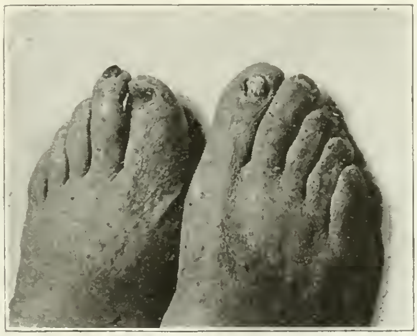

Fig. 3.—The toes before avulsion of the second left toe-nail (author's case).

Microscopic Examination of Scrapings.—On the first occasion the material was selected from the crumbly matter beneath the free margin of the right great toe. To my suprise no mycelia, but double-contoured bodies were discovered which suggested the possibility of blastomyces (Fig. 4). In a second preparation very fine mycelia were found (Fig. 5). On a second occasion I examined material from all three of the diseased toes. This time mycelia were found in all, and some of the double contoured spores in addition in the material from the right great toe, i. e., in the same location they were found in before. There was, as usual in toe-nail scrapings, nothing characteristic about the mycelium which could not be explained on the basis of variations in involution. In some preparations it was broad and in others narrow, according to the differences in age, sufficiency of nutrition and vigor of growth of different specimens. On a third occasion all ten nails were examined. This time the double contoured conidia were found in the two largest toes of the right foot, and nowhere else. Mycelia and small spores were found here and also in the other great toe.

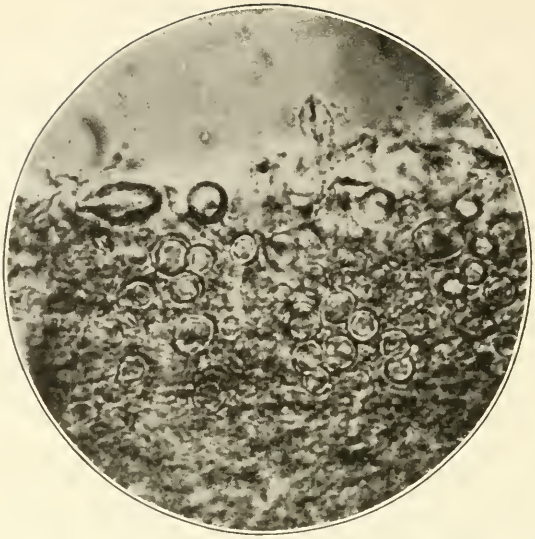

Fig. 4.—Scrapings treated with 10 per cent. sodium hydroxid solution and examined fresh. Note double contour of the spores.

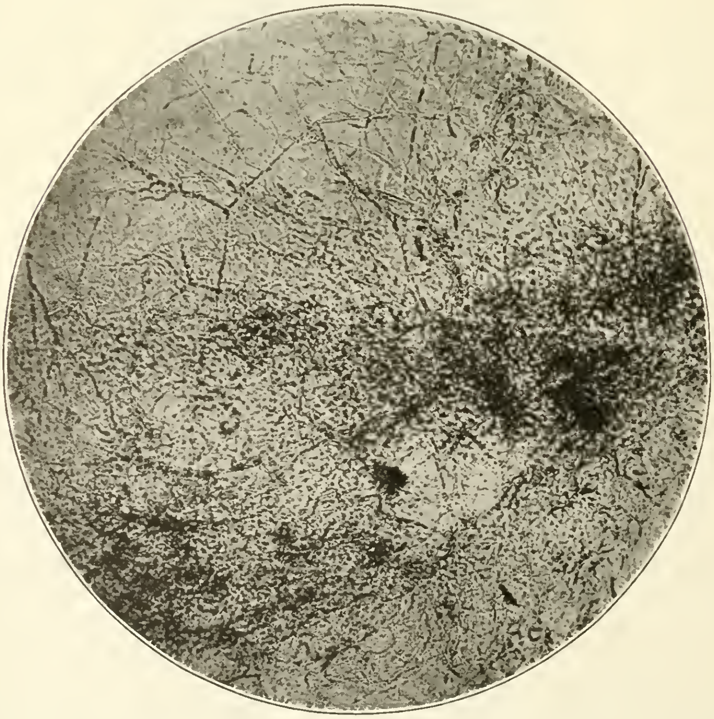

Fig. 5.—Scrapings in 10 per cent. sodium hydroxid solution. Very low power, showing delicate character of mycelium.

The double contoured conidia, as found in extemporaneous potash preparations, were for the most part scattered in small groups through the preparation, but occasionally in denser masses. I have never observed them in penicillium branchings here in scrapings, however, as did Brumpt. They measured from 6 to 8 mm. in diameter, were faintly yellow, spherical and had a thick double membrane. The interior was hyaline and structureless, in others finely granular.

On careful examination, some of the spores (those lying in the appropriate plane) exhibited a slight flattening or pouting at one point which corresponds to its point of attachment to the original mycelium from which it sprang. It thus came to take on something of the appearance of a huckleberry, and reminded one of the operculation seen in ova of some of the parasitic worms (Fig. 11).

CULTURAL STUDY

Three series of cultures were made directly from the case at about monthly intervals. The first was from scrapings under the right great toe nail, the second from the three diseased nails, and the third from all ten nails—the scrapings from each nail being cultivated separately. From the first series a number of obvious contaminants (*Pencillium glaucum*, etc.) was obtained, and *P. brevicaule*. From the second and third series no less than nine different species of mold were obtained—consistently the same in each toe in each of the two examinations; but *P. brevicaule* was not obtained in the two latter series. Of the nine species, several were common saprophytes, but others appeared strange and have not been sufficiently worked up to report on. The details of *P. brevicaule* have been worked out, however, and the chief purpose of this paper is to record them.

Method and Materials.—This description is based on cultures made on plain, glucose, Sabouraud's proof, and Sabouraud's peptone (conservation) agars and on Petroff medium. The organism was grown in various sized test tubes, Petri dishes and hanging agar block (microscopic) preparations. I have insured purity of culture by using fishings from a colony that was microscopically observed to germinate from one of the double contoured conidia like those originally observed in scrapings, and which at no time came in contact with other colonies of any sort (Fig. 6). Descriptions are from growths on mediums and contained strictly according to Sabouraud's formulas, but from ingredients of American manufacture.

Naked Eye Appearance.—Growth was visible within twenty-four hours on all the mediums above named. In the recently isolated cultures the colony was not distinctive until the fifth day, when it became coco-brown. Color developed a little more quickly (on the third or fourth day) after repeated subculture.

In the meantime it was grayish-white and delicately fuzzy. The distinctive brown color developed more rapidly when there was a thin layer of medium, as in the Petri dishes—even when drying out was prevented by hermetically sealing. The deepest shade of brown, which was about that of an unsweetened dry coco, developed (and most speedily) on glucose agar. The margin was regular, and while definite, was not sharp (Fig. 7).

Morphology is best studied in the large (potato) tubes recommended by Sabouraud or the duplex Petri dishes devised in this laboratory, by both of which thick strata of medium are made available. A solitary point should be inoculated—not a streak.

In these containers the brown color (and at the same time powdery surface) became barely recognizable in three days on glucose agar, in four on plain and proof agars, in five on conservation, and in six on Petroff's. It became strong in the course of two more days, but showed differences in intensity when the colony became fully developed, which required about two weeks. At this time the color on both plain and glucose agar was strong yellowish brown, the latter being slightly more colored than the former. On conservation agar it was a pronounced fawn color, on Petroff's, a dirty blackish brown. On proof agar the colony was dirty brownish gray as long as the medium remained very moist, as at the bottom of the tube. Only as it dried out did it take on the stronger dirty gray brown color. Color extended almost fully to the margin of the colony except on proof agar. On the latter it was variable—occasionally covering the whole surface, but generally important only in the center. Elsewhere it was dirty gray.

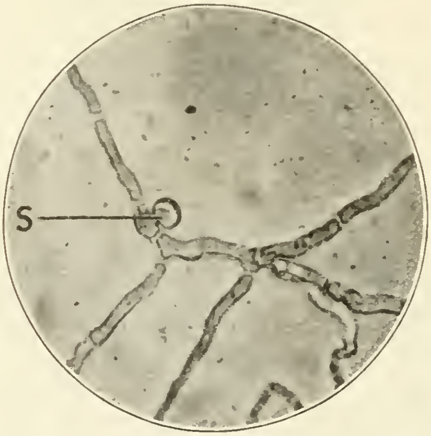

Fig. 6.—Spore of *P. brevicaule* isolated from scrapings, germinated and giving rise to mycelia. The spore is a little too much out of focus to show its double contour.

Luxuriance also varied on the several mediums. In four days glucose agar colonies were 25 mm. in diameter, a little smaller on plain, proof and conservation mediums, and but from 10 to 15 mm. on Petroff's. The thickness of the colony was also greatest on glucose agar, leading to the production of radial folds in five days. Similar folds developed on the other mediums when they reached a comparable stage of luxuriance, except for plain agar, on which they never developed. Here the colony was always thin and flat—even when a month old. The folds were never numerous—not more than a dozen—except on proof medium. On this there sometimes were as many as thirty at the end of three weeks, and by this time fissures appeared between them—mostly radial—but occasionally transverse near the center of the colony. The depth of these fissures was variable. They were never deep under any circumstances except on proof agar; and became so deep on the latter in four weeks as to separate completely the culture mass and display the medium underneath.

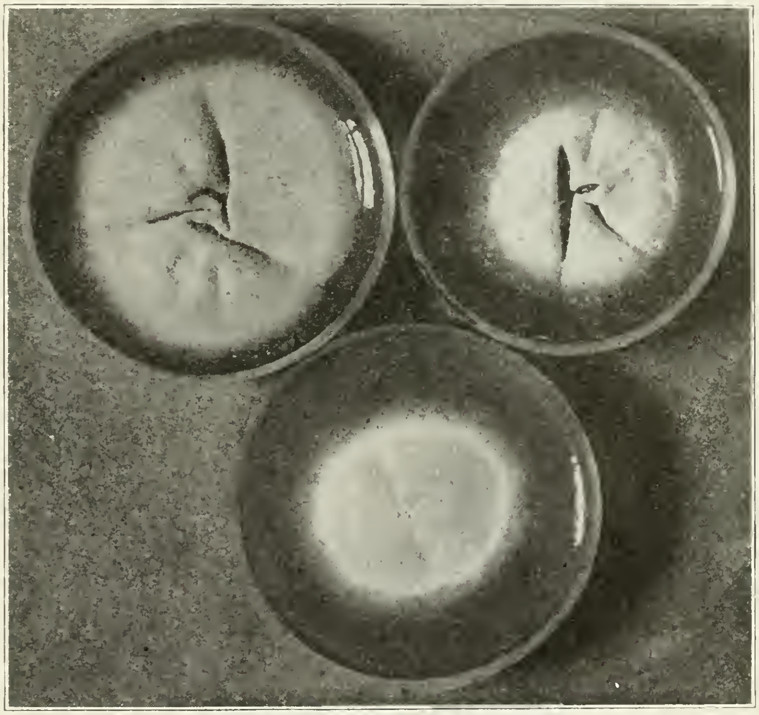

Fig. 7.—Culture full size; upper two on Sabouraud's proof medium; lower on conservation. All are 3 weeks old, planted on a thick stratum of medium and reared identically. Note difference in depth of the furrows, amounting to fissures on the proof medium.

Microscopic Appearance In Hanging Conservation Agar.—In twenty-four hours a conidium was found to have "germinated" and from it a branched mycelium already extended (Fig. 6). At first colorless, in forty-eight hours the mycelium took on a decided greenish color by transmitted light. As yet no conidia or spores had developed. In sixty-four hours the colony was 8 mm. in diameter. By this time intercalated chlamydospores had formed and the ends of some mycelia had become clubbed, suggesting early fuseaux formation. On the fourth day conidia (spores) began to appear. At first they were solitary (Fig. 8), and projected as buds directly from the mycelium both terminally and laterally, but later secondary conidia budded out from

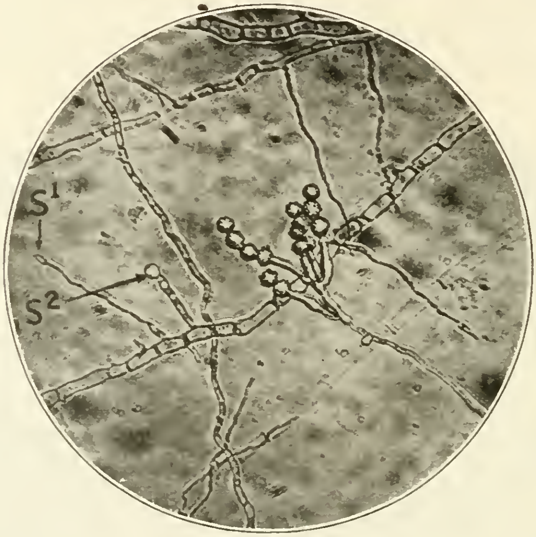

Fig. 8.—Hanging agar preparation (photomicrograph); growth about 2 weeks old. Earliest spore development at S^1; later at S^2. Typical sporangium in center of illustration. Strings of spores still attached to hyphae—contra Figure 12.

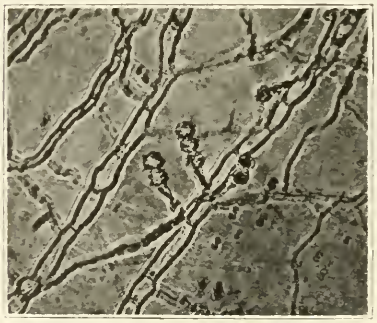

Fig. 9.—Budding of spores in single chain.

them in a way suggestive of yeasts (Fig. 9). The whole aspect of the colony up to this point was like that of one of those yeasts that develop mycelia in culture.

The buddings continued until on an average a chain of seven or eight conidia had been formed. I have counted up to seventeen. As they multiplied, slender non-segmented hyphae generally developed from the parent mycelium to support them; often the hyphae were thick and segmented. In the earlier colonies there was no grouping of hyphae into penicillium types—these developed only in older colonies, those two or three weeks old. At this stage they extended singly from the parent mycelium like S^1 and S^2 in Figure 8. Conidiophore hyphae have the same greenish color by transmitted light that the spores have, and brown by reflected light.

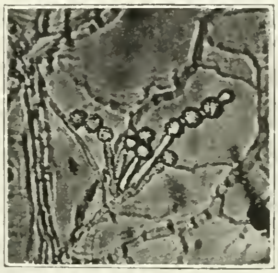

Fig. 10.—Early (terminal) structureless spore budding from neighbor. Note also the jointlike intervals at intersections of some spores.

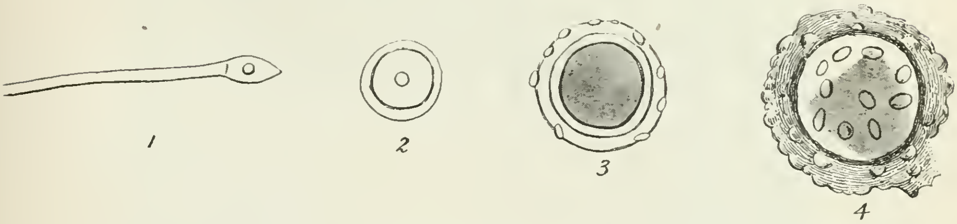

Fig. 11.—Drawing of spores, unstained. All have a greenish cast: 1, very early; 2, later—no granules as yet developed, hyaloid and structureless throughout; 3, beginning development of granules; 4, fully developed spore; granules very coarse; central hyaline part lumpy or distorted. The (ten) ellipsoidal bodies are on the *surface* of the spore, not in its interior.

Fully developed conidia measure from 6 to 8 microns in diameter, and young forms from 5 to 6 microns. When the conidium first budded it was a structureless, glassy, greenish spheroid (Fig. 10). As it enlarged a double contour developed and coarse greenish granules appeared on the exterior. The center remained hyaline, however, as determined by careful focusing; although it might appear granular to superficial observation as a result of the overlying and underlying surface granules (Fig. 11). Stained by methylene blue, the center became strongly blue, while the "shell" and its granules took the color faintly or refused it, i. e., they retained their original greenish cast. Where attached to each other or to the parent hypha, they were often flattened and the double contour disappeared. They were loosely attached to each other, and on this account it was impossible to scrape a chain from the culture medium to a glass slide for photographing, or to obtain an "impression" preparation of them on an albuminized coverslip (Fig. 12). The accompanying photographs, which show chains of conidia, are of living colonies on "hanging agar" preparations. As the colony became older and dried out, the conidia ceased to bud further and became more thickly covered by granules which were much coarser than at first; as a result, the conidia became uniform in size throughout the chain, and comparatively opaque (Figs. 13 and 14). At the same time, hyphae became branched into typical penicillium form. These were never complicated, generally consisting of seven or eight branches; indeed, frequently these were so widely separated from each other as to require foreknowledge to appreciate that they were really penicillium groups (Figs. 8, 10, 12 and 13). Brumpt recognized the latter indefinite, or lack of, grouping, as indicated in both of his figures, but he does not comment on it. It is important taxonomically.

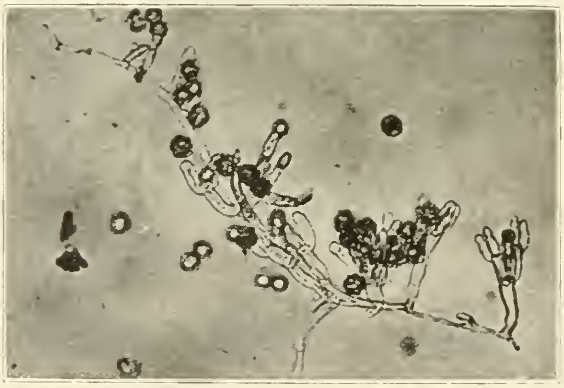

Fig. 12.—Appearance of sporangia scraped from growth; practically all the spores shaken off. Stained with methylene blue. Compare with Figure 2.

ANIMAL TESTS

A thick emulsion of spores and mycelia was injected both intravenously and subcutaneously into rabbits (two), guinea-pigs, white rats, white mice and pigeons. No lesions developed, with the exception of foreign body tubercles on the peritoneum; and cultures from heart's blood and peritoneum were sterile eight days after inoculation.

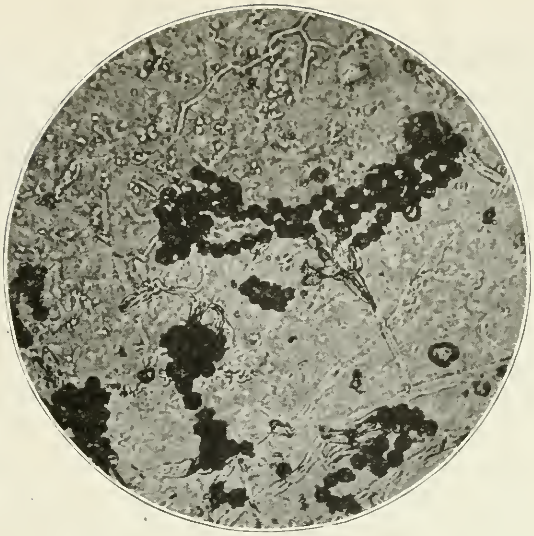

Fig. 13.—Old dried out culture; sporangium with long chains of deeply pigmented spores.

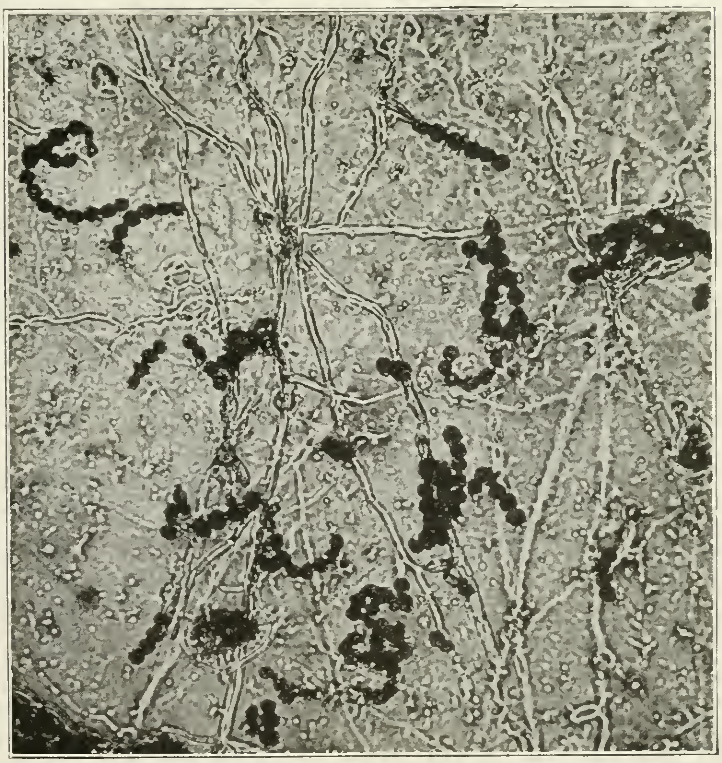

Fig. 14.—Old dried out culture; individual chains of various lengths with deeply pigmented spores. Suggests a monilia in the absence of the typical penicillium corymbs.

Fragments of culture were rubbed under all four great nails of two rhesus monkeys and under the great nails of a human being. No disease developed in any case. In the human case *P. brevicaule* was recovered in culture up to eighteen days after being rubbed in. The next culture was not made until thirty-eight days after inoculation, when it was negative, and has since remained so.

PATHOGENICITY

I cannot claim any pathogenicity for *P. brevicaule*. On the other hand, if limited to my own experience with this one case I would have to reject the idea, not so much on the basis of the negative animal experiments, although these have a certain weight, but mostly because the organism was so inconstantly recovered in cultures, and because so many other organisms were also, and more constantly, found. It will be recalled that Weil and Gaudin also found many different species of fungi in their cases. Why should we single out *P. brevicaule* from the host of others and fasten on it the burden of guilt? But Brumpt's results—five pure cultures in five trials (a remarkable result from such a position as the toe-nail)—cannot be overlooked or dismissed, and therefore it appears to be saner to regard my own results as only modifying our ideas as to its pathogenicity. It will be better to hold our minds open to further light before coming to a final conclusion.

SYSTEMATIC POSITION

There can be no doubt that penicillium groupings are present with this organism—and if the generic diagnosis rests solely on this point, the generic name given it is valid.[3] If, on the other hand, the original genus was based on the presence of these branchings alone and did not include also the individual chains which are present in *P. brevicaule*, there are ample grounds for considering the propriety of indicating a new genus.

The final decision on this point I prefer to leave to the systematist, who can investigate the original type species and compare it with the organism I have studied. Systematists are so constantly renaming and rearranging supraspecific groups that it would be an assumption for any one—biologist, pathologist or dermatologist—to attempt a new name on the basis of a single observation.

As to the specific diagnosis, there is every probability that the organism I have studied is the same as that originally described by

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[3] Saccardo, D. A.: Sylloge fungorum, Berlin, R. Friedlander & Son, 1886, p. 78.

Saccardo,[4] and figured by him in color.[5] It is certain that it is the same variety as that described by Brumpt and Langeron. The difference between the certainty and probability above implied depends on the difference between Brumpt and Langeron's variety and Saccardo's original one. I have referred to Saccardo's original works and find that his material came from decaying leaves in Italy and that, as figured, the mold (on a plant stem) had a faint brick red color instead of the yellowish brown which appears on our laboratory mediums. Drawings of mycelia, including sporangia, are of the same tint.[6] Otherwise, as far as Saccardo's data are concerned, my organism might be the same as his. It is therefore best to accept Brumpt and Langeron's variety, but in naming it to recognize Saccardo as the originator by prefixing his name and date to Brumpt and Langeron's. *P. brevicaule* is an interesting organism in other respects. First, at an early stage of its growth it shows fructifications like those of monilia and at a later stage those of both monilia and penicillium. Secondly, its conidia agree structurally and tinctorially with those of some monilia (Montoyai). It may thus prove to be a connecting link between the genera monilia and penicillium which may be useful taxonomically.

SUMMARY

A case of ringworm of three toe-nails on two feet is described, in which the scrapings were studied microscopically and cultivated. Mycelia and blastomyces-like spores were found in scrapings, and nine different species of fungi were isolated in cultures. Among the fungi a coco-brown penicillium was isolated, but as it was only cultivated once out of three trials and produced no disease on injection into and inoculation on animals, the author is inclined to question its pathogenicity. This report concerns only *P. brevicaule* and deals particularly with its morphologic and cultural characteristics.

I report the organism for the first time in the United States with a habitat under diseased nails with many other fungi, and add details of its cultural characteristics. I also bring out an important clinical point in that conidia of some fungi resemble and might be mistaken for blastomyces in scrapings.

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4. Saccardo, D. A.: Michelia, **2**:547; also in Sylloge fungorum, **4**:84.

5. Saccardo, D. A.: Fungi italici, July, 1877.

6. I have tried to cover this point by growing my strain on both solid and fluid mediums in which decaying leaves were mixed and also on moist and decaying leaves—both sterilized and unsterilized. In no case did I get reddish growth such as Saccardo reported (rubescentia) and figured.

DERMATOBIA HOMINIS *

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With the increasing extension of our commerce into the South American countries it is likely that more and more tropical parasitic diseases will be introduced into the United States. These will be of two types. The first will include only imported cases, in which some factor in the life history will be wanting in northern climates, and the life history of which cannot be completed here. These diseases will, of course, never get a foothold north of Mexico; they will be contracted in the tropics, although in the United States physicians will be called on to diagnose or treat the condition. The second, and far the worst type, will be the diseases for which material and conditions for the completion of their life cycle will be favorable in the United States. These are the most to be dreaded and demand the most careful consideration on the part of health officers, physicians and the public. To the first type of parasitic diseases belongs that condition caused by the larvae of *Dermatobia hominis*.

If the recorded incidence of infection by *Dermatobia hominis* in the United States is to be regarded as evidence, its occurrence must be very infrequent. Ward [1] has published a very excellent monograph on the subject, reviewing all the cases up to that date and definitely showing that the disease known as "ver moyoquil," "ver macaque," "torcel," "muche," "berne," etc., is caused by one species of larva, so that *D. noxialis* and *D. cyaniventris* are synonyms of *D. hominis* (Say).[2] In his collection of cases, he found that the first reported from the United States was by Say,[2] describing the case of Dr. Brick, who contracted the disease while traveling in South America. The second case was reported by Penniston,[3] who removed a larva from a sailor in the Charity Hospital in New Orleans. The sailor had acquired the parasite while traveling in Vera Cruz and Tabasco, Mexico. Matas [4] reported the third case, that of an Englishman from Spanish Honduras, who was operated on in New Orleans, three larvae being removed from the gluteal region. In this paper he refers to a previous case, that of a Frenchman, also from Honduras, in the Charity Hospital. Blanchard[5] refers to three or four cases from America; they were, however, reported to him in the form of personal communications. These are all that had been recorded up to 1903, and I have been able to find but four in the American literature since that time.

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* From the Section on Clinical Laboratories, Mayo Clinic.

[1] Ward, H. B.: On the Development of Dermatobia hominis, Mark Anniversary Volume, Article xxv, 1903, pp. 483-512.

[2] Say, T.: On a South American Species of Oestrus which Inhabits the Human Subjects, New Orleans M. & S. J., 1844, p. 23.

[3] Penniston, T.: A Case of Malis Oestri, or Gadfly Bite, Occurring in Human Subjects, New Orleans M. & S. J., 1844, p. 24.

[4] Matas, R.: Report of the Case of a Patient from whose Subcutaneous Tissue Three Larvae of a Species of Dermatobia were Removed, with Remarks, New Orleans M. & S. J., **15**: 161, 1887.

One is reported by Brooks[6] in 1905. The patient had been in Panama and in good health. Six weeks before presenting himself for examination he noticed three small lumps, one in the groin, one on the flexor surface of the forearm and the third over the left shoulder. Each tumor showed at its apex "a small perforation through which a small, moving, black body could be made out." There was a great deal of local pain and a slight rise of temperature. The tumors were opened and the "worms" squeezed out. The largest was 2 cm. long and 9 mm. in breadth. The wounds healed rapidly. There was a marked increase of eosinophils in the blood.

In discussing the case, Dr. James Ewing said that Dr. Alexander Lambert had sent a similar parasite to the Cornell Laboratory which had been removed from a patient, who had recently come from Panama.

A second case was reported by Costa.[7] He was asked to see a child who was returning on a boat from Tiberiza to Brazil. The child had been living for ten months in the former place and had recently developed three tumors on her head. These were roundish and of "the size of a small mandarin." Costa expressed from each a larva of Dermatobia. While the case was reported in a North American journal, it is quite evident that this is not in any sense a North American case.

The third case, reported by Singleton,[8] is that of a German who had lived for six months as a tramp in Mexico. He presented himself to a physician in Galveston, Texas, with a tumor on the dorsum of the penis just behind the glans. The swelling was "as large as a pecan," felt hard and was only slightly inflamed. It felt more like scar tissue than anything else, and a little pus and serum exuded from a central depression. The patient said that flies were very common in parts of Mexico where he had traveled and that he had been bitten on the penis while bathing. From the center of the mass Singleton extracted a larva of Dermatobia about three fourths of an inch long.

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[5] Blanchard, R.: Contributions a l'etude des dipteres parasites, Ann. Soc. entomol., **65**: 641, 1897.

[6] Brooks, H.: A Case of Dermatobia Noxialis, with Demonstration of Larva, Med. News, New York **86**:430, 1905.

[7] Costa, E.: Two Important Parasites of the Skin, J. Cutan. Dis. **28**:24-32, 1910.

[8] Singleton, A. O.: Report of a Case of Dermatobia Noxialis in Man, J. A. M. A. **58**:1282 (April 27) 1912.

The last case, reported by Dunn,[9] was that of Dr. Clark, who became infected while making a tour by way of the Boqueron River in the interior of Panama. He noted on returning to camp that he was acting as a host for a certain species of tick, and later at the site of the tick bites developed inflamed wounds, exuding serum. In each was found a larva of *Dermatobia hominis.* A few months later while huntng near Arraijan on the west side of the canal he became infected a second time, a tick attaching itself to the right side of the abdomen. About three weeks afterward, he removed a larva of *D. hominis* 2 mm. in length, from the point of the tick bite. This incidence is offered by Dunn to demonstrate that the tick of the species *Amblyomma cajennense* is capable in some way of acting as a carrier for the eggs, and is "also instrumental in assisting the larva to penetrate the skin." This is interesting, and should be further investigated, since practically all authors have believed the parasite requires some species of mosquito as a vector during its life cycle.

I am deeply indebted to Dr. A. E. Mahle of the Mayo Clinic for turning over to me a larva of *Dermatobia hominis* which had been sent to him by Dr. Donna M. Parker of Peoria, Ill. This had been extracted from a patient whose history is presented herewith.

REPORT OF A CASE

Mr. W. F. H., aged 28, of Jacksonville, Ill., had been in the tropics from June to September, 1917, from January to July, 1918. from March to September, 1919, and from December, 1919, to March, 1920. Except for occasional headaches and one attack of malaria, he had been in good health. He had been in Panama about one week when he noticed a local sensation in his shoulder like a sharp pin prick. Five or six days later, a rather painful boil appeared which several days later appeared to be a carbuncle. He applied cataplasm of kaolin; the mass came to a head and a physician lanced it and removed a "worm" and a quantity of yellow pus and dark blood. Later the patient himself extracted a worm from another site. He had been in the United States a short time when he had other abscesses. Dr. Parker opened these, removed the larvae and packed the opening with phenolated gauze. The patient says the treatment was entirely satisfactory and that he has had no further trouble.

DESCRIPTION OF PARASITE

The worm which the patient himself extracted is shown in Figure 1 and is enlarged about three times the normal size. Actually it is 9 mm. long and 3 mm. wide at its greatest diameter. It is

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[9] Dunn, L. H.: The Tick as a Possible Agent in the Collocation of the Eggs of Dermatobia Hominis, J. Parasitology **4**: 154, 1918.

white, and the rows of black hooks stand out sharply. The anterior portion is about 3 mm. long, the posterior 6 mm. I can agree with Ward in his description of the arrangement of the hooks. The first, second and third somites bear each a row of small hooks; the first has the smallest. The fourth somite has a complete row of hooks anteriorly with a row of larger ones posteriorly, interrupted ventrally. The fifth and sixth segments have anterior complete and posterior incomplete rows of hooks, while the seventh has only an anterior complete row. The body tapers posteriorly from the last row of hooks, until it is about half a millimeter in diameter. The terminal portion of the larva is inrolled and the exact nature cannot be described.

The tenth somite is in the form of a collar and is covered with minute hooks. These are not black, like the hooks of the anterior somites, but are reddish brown. The last somite is retracted into the collar formed by the tenth. The first bears the two mammiform protuberances on the dorsal surface described by Ward and the single pair of mouth parts which consist of conspicuous heavy black hooks bent in a ventral and posterior direction. Minute description of the hooks and somites is omitted, for it would be merely a repetition of the excellent description of Larva A given by Ward, which was of about the same size as the one I studied.

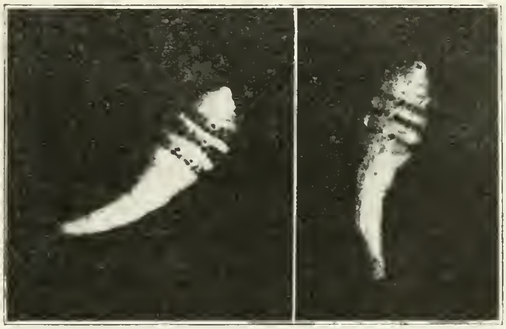

Fig. 1.—Larva of Dermatobia hominis: *A*, dorsal view; *B*, ventral view.

GEOGRAPHIC DISTRIBUTION OF THE PARASITE

The distribution of the parasite is as follows: Brazil, to 18 degrees south latitude and west to the mountains, French and British Guiana, Venezuela and the Island of Trinidad, Colombia and Peru. Records are found of its occurrence in Costa Rica, Honduras, Guatemala and certain Mexican states. It occurs westward of the great mountains on the Pacific coast. It does not appear on the great central plateau of which the altitude is excessive and the mean temperature insufficient.

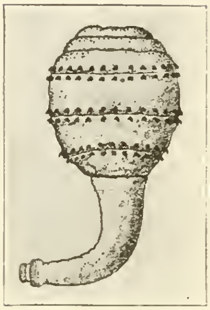

Figure 2

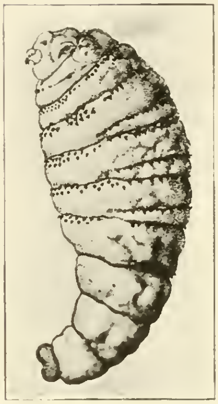

Figure 3

Fig. 2.—Young larva of Dermatobia hominis, × 3. (After Castellani and Chalmers.)

Fig. 3.—Older larva of Dermatobia hominis Macquart, × 2½. (After Castellani and Chalmers.)

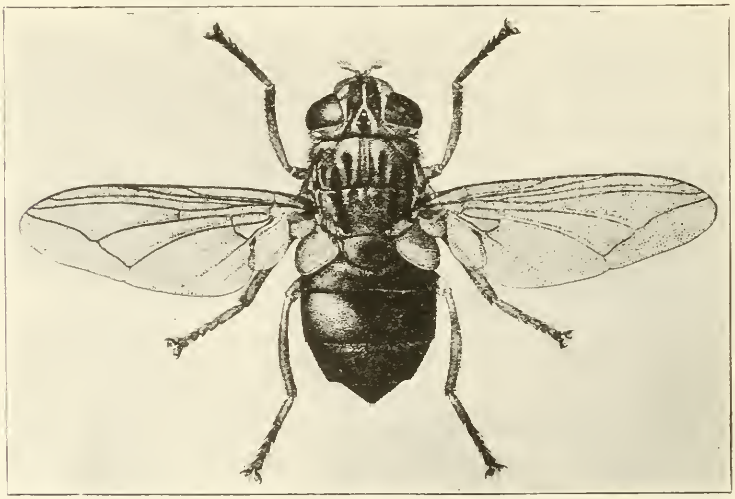

Fig. 4.—Dermatobia hominis Macquart, × 3. (After Castellani and Chalmers).

It is interesting to note that while it does occur very close to the southwestern border of the United States, no cases have been reported in which the disease has been contracted within this country. Blanchard tried to locate incidences of the infection by extensive correspondence with societies and individuals in Texas and Louisiana, but failed.

The larvae have been found in the flesh of many different kinds of animals, including cattle, pigs, dogs, mules, agouti, jaguars, monkeys, toucans, ant-thrushes and man.

There is still much work to be done on the life history and mode of transmission of the parasite. The natives of many of the countries in which the infection is found call the larvae mosquito worms and think that a mosquito of the genus Psorophora is responsible for the infection. Surcouf has found these fly larvae cemented to the mosquitoes of the genus Janthinosoma, a very vicious biter. It is possible that the young larva escapes from the mosquito as it bites, and takes up its habitat in the skin of the victim. The young larva is at first club-shaped and is then known as "ver macaque." Later it becomes worm shaped and is known as "torcel" or "berne." The larva described above is older than a ver macaque but not yet developed to the stage of the torcel (Figs. 2 and 3). If not interfered with, it remains in the skin until an abscess forms and the larva is thrown out, drops to the ground, pupates, and finally develops into the imago. The adult fly is shown in Figure 4, and is known as a "gadfly." Typically the larva causes local pain and itching, with swelling, and edema of the surrounding region, "giving rise to a boillike swelling, rather hard, of a deep red color, with a central opening." Here one sees at times the stigmas of the organism, and it may appear or disappear like a jack-in-the-box. The Brazilians try to kill the larvae with tobacco smoke, or apply fat to the opening to cause asphyxiation. They are easily extracted with sterile forceps, the wound opening enlarged and the swelling treated in essential respects as a furuncle. By the last method recovery is usually rapid and satisfactory.

ANAPHYLACTOID DERMATITIS DUE TO DIRECT CONTACT WITH ANIMAL EPIDERMAL STRUCTURES *

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In a recent paper dealing with certain cutaneous manifestations of anaphylaxis, a well known writer [1] states that "the cutaneous phenomena which occur as a result of the absorption of foreign proteins through the respiratory tract and possibly through the skin itself have not received the attention and study that they deserve." This statement, combined with a recent illuminating experience of my own, has prompted the presentation of this brief paper on a phase of this subject which is, I believe, of definite clinical interest, namely, that the skin alone, and even limited areas of the skin, may be sensitized by and react to direct contact with specific substances contained in the epidermal structures of certain animals, as shown in the following case report.

REPORT OF A CASE

History.—Mrs. R., aged 39, an office assistant, came under observation Feb. 2, 1919, presenting a skin eruption of six months' duration, during which time she had been under constant treatment. Her previous history was irrelevant and she made no complaint aside from the skin disorder.

Examination.—This revealed an erythematous and papular eruption involving practically the whole of the face, neck and chest, the anterior surfaces of the forearms and the cubital spaces; the hair was harsh and dry, the scalp scaly but not actively inflamed. There was considerable swelling about the eyes and areas of weeping surface over the lids and at the angles of the nose. Itching was intense, particularly at night, and the duration of the condition had induced marked nervous disturbance.

Treatment and Course.—The distribution of the eruption and the appearance of the scalp suggested a seborrheic dermatitis and treatment was begun with that diagnosis. Some evidence of digestive disturbance led to careful regulation of the diet, which, with mild local applications, brought about prompt improvement; this was, however, only temporary. About March 1 an examination of the mouth disclosed a number of alveolar abscesses and definite pyorrhea for which she was placed under the care of a competent dentist; this also resulted in temporary improvement. During the succeeding few months repeated inquiry was made as to a possible external source of irritation—plants, chemicals, etc.—but none could be discovered, and on June 1, nearly one year after the beginning of her difficulty, her condition was worse than ever, notwithstanding constant efforts to determine the cause of the disorder and to relieve it by treatment. A gastro-enterologist was then consulted, who discovered an absolute achlorhydria, and she was put on strict diet again with seeming benefit. Another internist discovered a chronically inflamed appendix, and this was removed on Sept. 1, 1919. During her stay in the hospital the skin cleared up completely and it was believed that relief was permanent; on her return home, however, the eruption recurred with increasing violence. The patient was now reduced almost to desperation and was frequently unable to attend to her work. Relief came unexpectedly through her own discovery that the skin always became immediately worse after cleaning out the pen of a guinea-pig belonging to her small son and allowing it to run about over her shoulders. Disposal of the animal was followed by prompt and permanent disappearance of the eruption and complete clearing of the skin, and now, eight months later, there has been no recurrence.

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

[1] Sutton, R. L.: Ragweed Dermatitis, J. A. M. A. **73**:1433 (Nov. 8) 1919.

Tests to Determine Specificity of Reaction.—After discovery of the cause of this eruption and its complete disappearance, numerous tests were made to determine the actual specificity of the reaction, this being done by binding firmly on the skin patches of animal hair and leaving them for definite periods. The first test made with guinea-pig hair applied to the side of the neck for four hours gave a strongly positive result with local vesication and an erythematous eruption, which within twenty-four hours had spread over the front of the chest, the chin and lower part of the face on the same side, subsiding in about three days. Repetition of this test on various parts of the body soon showed that the skin never involved in the original eruption always gave a negative result, even after six hours' application, while the skin of areas previously affected gave a positive result after two hours' application of guinea-pig hair. Control tests made in each instance on another person, and similar tests made with hair of other animals—cat, dog and horse—were all uniformly negative, the last series being completed on April 10, with a final positive result.

SKIN SENSITIZATION

In so far as this case may be accepted, it seems to prove that circumscribed areas of the skin may be sensitized by and react to direct contact with substances which are without effect on the normal skin. This is, of course, not an original observation, von Pirquet[2] in his early work having noted that the skin of his left arm, which he habitually used for experiments, was sensitive to a tuberculin dilution of 1 : 1,000 while the skin of his right arm was negative to tuberculin ten times as concentrated.

Hay fever, too, is regarded by some observers[3] as a definitely localized sensitization of the epithelium of certain mucous surfaces, reaction occurring only on direct contact with the sensitizing agent, and further that desensitization can be accomplished only by local application of a specific vaccine.

The manifestations of cutaneous hypersensitiveness, as ordinarily observed, consist of hyperemic and urticarial eruptions of general distribution and relatively low grade activity, resulting from the action on the cutaneous tissues of specific substances carried by the circulating fluids in necessarily minute amounts. Such reactions, however, induced by local application of the sensitizing agent, are more violent because of the greater concentration of the antigen, and it is probable that in the cases of rag-weed dermatitis reported by Sutton[1] and Hannah,[4] the acute inflammation of the skin was due to direct contact with pollen, even though sensitization resulted from absorption through the respiratory tract. Similar instances are frequently observed, such as attacks of asthma or hay fever following close proximity to certain animals, with coincident development of acute dermatitis on areas of the skin brought into direct contact with the animals.

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[2] Zinsser: Infection and Resistance, New York, Macmillan Co., p. 445.

[3] Zinsser: Infection and Resistance, New York, Macmillan Co., p. 437.

SKIN SENSITIZATION AND ANAPLYLAXIS

The relation of skin sensitization to the more general condition known as the "anaphylactic state" is at present not clear. Since it is well known that the skin may be sensitized by many substances non-protein in character, the resulting cutaneous phenomena are held by many observers not to be true manifestations of anaphylaxis. It has been definitely shown, in a recent paper by Fleischner[5] and others, that the highest degree of anaphylaxis may be induced without the coincident production of cutaneous hypersensitiveness. It is possible, therefore, that such phenomena are not antigen-antibody reactions, but purely skin responses to stimuli rather of the nature of toxins, yet their definitely specific character so closely resembles that of anaphylactic reactions as to justify the application to them of the term anaphylactoid.

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[4] Hannah, L.: Ragweed Dermatitis, J. A. M. A. **72**:853 (March 22) 1919.

[5] Fleischner, E. C.; Meyer, K. F., and Shaw, E. B.: A Résumé of Some Experimental Studies on Cutaneous Hypersensitiveness, Am. J. Dis. Child. **18**:577 (Dec.) 1919.

SO-CALLED DERMATITIS DYSMENORRHEICA

REPORT OF A CASE, WITH REVIEW OF THE LITERATURE

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Ever since the publication of the article by Matzenauer and Polland[1] dealing with a peculiar dermatosis occurring in women having dysmenorrhea and manifesting itself during the menstrual periods, there has been much controversy among dermatologists with regard to the *genuineness* of this affection. The authors describe what they consider to be an entirely new entity. Similar cases had been previously observed and recorded, but they were classified under the hysterical dermatoses, dermatitis artefacta, malingering, etc., that is, the self-inflicted dermatoses. A detailed description of five cases of the new disease is given.

One of these was the subject of a careful study made by Kreibich[2] antedating the observations of Matzenauer and Polland. Kreibich believed that the disease manifestations were due to a reflex neurosis, provoked by increased irritability of the dominating vasodilator center. His studies led him to advance the theory of a so-called angioneurotic inflammation.

On the basis of their studies, Matzenauer and Polland offered a totally different interpretation of the pathologic processes involved in the causation of this peculiar dermatosis. All of the patients were women afflicted more or less with dysmenorrhea. The eruptions consisted of spontaneous, usually symmetrical lesions affecting the face, trunk and extremities, occurring in the form of erythematous patches, urticarial wheals, but more often, vesicular eruptions resembling ordinary weeping dermatitis. Some of these lesions underwent spontaneous necrosis. In some of the patients, the necrotic efflorescences were distinctly linear in configuration, clinically indistinguishable from the linear self-inflicted injuries of malingerers. Other lesions were strikingly limited to the follicular appendages of the skin. A goodly number of pages in this long article are devoted by the authors solely to the demonstration of the fact that these apparently artificial and self-inflicted formations are in reality *spontaneous* in nature. Physical

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1. Matzenauer, M., and Polland, R.: Dermatitis Symmetrica Dysmenorrheica (A Contribution to the Angioneurosis Question), Arch. f. Dermat. u. Syph. **111**:385, 1912.

2. Kreibich, C.: Die Angioneurotische Entzuendung, Vienna, M. Perles, 1905; Die Angioneurosen und die haematogenen Hautentzuendungen, Arch. f. Dermat. u. Syph. **95**:405, 1909.

examination of some of the patients revealed the coincident occurrence of cardiac vasomotor disturbances, circulatory abnormalities and psychoses. Taking into consideration the hysterical element, and realizing the difficulties in the handling of this class of patients, the authors describe with the greatest precision the various precautions which they took to rule out every possibility of malingering. Among these was, of course, the guarding against self-inflicted injuries by means of stable and impervious bandages, etc. In one of the patients, the beginning of a lesion and its subsequent developmental stages were observed by one of the physicians, while the subject was fast asleep. Another woman visited the clinic just before a new patch began to appear on the skin, affording an opportunity to watch its progress and gradual development. Every possible bit of evidence is submitted by the authors to prove their contention that malingering plays no part in the pathogenesis of the different eruptions which they describe. It is their belief that the dermatosis is an expression of systemic disease, possibly the result of toxic metabolic products, due to derangement of the ovarian follicles.

Many excellent photographs accompany the article. These demonstrate all the different types of lesions described in the text: erythematous, urticarial, follicular, bullous, hemorrhagic, necrotic, etc., but above all, they illustrate with exceptional vividness pronounced lesions of *linear configuration* which, even to the inexperienced eye, seem to call loudly for the label "dermatitis artefacta." The dubiousness with which the entire contribution is regarded by many dermatologists may unhesitatingly be attributed to the actual, vivid portrayal of the linear formations accompanying the text. Those who regard the illustrations alone and decide to digest the lengthy text at some future and perhaps more auspicious time, instantly arrive at the conclusion that the illustrations represent the vagaries of hysterical women who purposely or unconsciously inflict various injuries on their skins. On the other hand, there are those who, not content with a view of the illustrations alone, suffer themselves to read the text as well. Be it said of these that the majority are by no means diverted from their prejudice in favor of an artificial eruption. To quote one eminent authority, to wit, Hartzell:

> Very recently Matzenauer and Polland, under the name dermatitis symmetrica dysmenorrheica, have reported a number of cases, occurring for the most part in young girls, characterized by linear patches of erythema and excoriations, wheallike lesions and exceptionally by superficial necrosis of the skin. A study of the history of these cases, and more especially of the excellent illustrations which accompany the report, leaves but little doubt in the author's mind that the eruptions were factitious.

Criticisms by other observers will be referred to later, more in detail.

In justice to Matzenauer and Polland's painstaking work, and in view of the fact that they state without equivocation that the lesions, despite their great resemblance to artefacts, are in reality spontaneous, it is only fair for us to devote some space to the consideration of the arguments, pro and con, which the authors submit in favor of their contentions. Taking the bull by the horns, they state in the very beginning of their article that in the earlier period of their studies they regarded with much skepticism the prevailing views entertained about the etiology of various angioneurotic cutaneous manifestations, and more especially with reference to the etiologic factors obtaining in the class of cases forming the subject of their report. They paid particular attention to the question of malingering, feigned eruptions, hysterical manifestations, etc. As a result of their studies they concluded that they were dealing with an "idiopathic, hitherto little known and insufficiently described disease, which in every respect presented a characteristic, typical course, and whose segregation (from other dermatoses) was justified on the strength of its probable etiology." As already stated, they included in their group of five patients one of Kreibich's "angioneurotic" cases; emphasis is laid on the statement that none of the other cases described by Kreibich is included under the category of dermatitis dysmenorrheica. The latter is to be strictly differentiated, not only from the angioneuroses of Kreibich, but also from all the different affections described in the literature under such captions as hysterical, neurotic, angioneurotic gangrene, spontaneous gangrene of the skin, zoster hystericus, herpes neuroticus, etc. In other words, they contend that they are dealing with a disease entity.

A detailed account of the authors' five cases makes interesting reading, but is too intricate to be recapitulated here. They draw a composite picture of the disease somewhat as follows:

A PICTURE OF THE DISEASE

The first thing the patient feels in the affected region of the skin is a burning sensation; all patients tell the same story. The intensity of the sensation varies greatly; often they are not even conscious of the burning, especially if the lesion begins during sleep, which often happens; at other times the sensation may be intense and prolonged. Coincident with this subjective symptom, the affected area presents an urticaria-like swelling, of a faint rose-red or pale eosin color, and the size of the fully developed lesion. The lesion is often more readily felt than seen. At times the original spot shows a peripheral zone of spreading erythema, while the central portion assumes a more marked urticarial aspect. The very faint, pale red tinge of the lesion differentiates it strongly from the more intensive scarlet redness of other inflammatory processes, such as traumatic or bacterial inflammations.

After a short while, from a quarter to a half hour, a further stage of development manifests itself: The follicular orifices stand out more distinctly, each one being surrounded by a very narrow anemic zone, simulating a perifollicular urticaria porcellanea; this appearance is soon followed—especially in the slowly progressing cases—by an exudation of serum into the funnel-shaped follicular orifice which it soon fills; subsequently a thin, yellowish-brown crust forms. All these manifestations are always strictly limited to the follicles. Later on, especially in cases running a more acute course, a superficial desquamation about the follicles ensues, leaving a vesicular zone around each orifice. The follicles being close together, these vesicular areas soon coalesce to form patches of weeping dermatitis or yellow crust-covered lesions, simulating traumatic excoriations. Some of these weeping patches have little zones of fine vesicles.

This process always runs its course within a few hours, acquiring its maximum of development in that time, resulting in the production of a lesion which is red and inflamed, weeping and partly covered with serofibrinous crusts. Owing to the diffuse edema, the patch is slightly elevated and is surrounded by a more or less well marked zone of erythema. The crusts are often brown, due to minute blood extravasations. The formation of the latter may be readily observed at the edge of a lesion, contiguous to the unaffected skin, where the perifollicular edema makes the follicular orifices much more prominent. The extravasations visibly take place about and into the mouths of the follicles. The filling of a dilated follicular orifice with a tiny drop of blood is sometimes actually observed with the naked eye. If the process of development is slow, the lesion appears merely as a patch of punctate follicular extravasations; if acute, there is a central weeping area, with a zone of these follicular formations.

The further manifestations are either of secondary nature or are the result of involution of the lesion. External influences, such as rubbing or scratching, may result in superficial excoriations or slight hemorrhages, thus intensifying the inflammatory process, causing increased exudation and crust formation. Thus the lesion may assume the appearance of a rather deep-seated excoriation. Usually the necrosis and the detachment of the epidermis reaches no farther than the rete malpighii; occasionally the process extends down to the papillary body, usually as a result of external injury. As a rule, healing occurs beneath the crusts within three or four days; but for some time after, the area presents a reddish spot, which later becomes brown, that is, distinctly pigmented. The same areas may, however, be affected in repeated attacks without leaving any traces.

In the more severe cases, the necrosis may extend deeply, resulting in the formation of hypertrophic scars and keloids. In these cases, a dry necrosis appears from the start, instead of a weeping surface. There is an anemic infarct, which at first is pale, later becoming distinctly brown from the blood pigment; the process of involution of these lesions, extending deeply into the corium or to the subcutaneous fat, is extremely slow, and is associated with a purulent exudate surrounding the necrotic mass.

As to the localization of the patches, any part of the body may be affected; the face is the area of predilection, the next most often affected parts being the hands, the trunk and the upper and lower extremities. In one of the patients, there was a coincident eruption on the tongue and buccal mucosae. The lesions are almost always symmetrical in distribution; they are usually round or oval on the cheeks and buttocks, while on the extremities they are linear in outline.

CAUSATION OF LESIONS

The question now arises, are these lesions spontaneous in nature or are they self-inflicted?

A series of experiments was carried out in Case 1, this patient being the same one whose case was reported by Kreibich as Case 4 among the "angioneurotic inflammations." Kreibich did not interpret the lesions as being a menstrual dermatosis associated with dysmenorrhea; he merely cited the case as one example of angioneurotic inflammatory dermatoses. Even at that, the great majority of dermatologists refused to believe Kreibich's statement that the lesions were anything but self-inflicted, much to that author's chagrin. At all events, Polland had this patient under his personal observation, not only during the period of Kreibich's supervision, but also for an entire year thereafter. In the course of that year, Polland had ample opportunity to satisfy his curiosity with regard to the question of malingering.

The lesions appeared under impervious dressings of "zinc-lime," so applied that it was impossible for the patient to practice deceit.

On one occasion, a lesion appeared at a certain time on the right leg. The analogous (unaffected) area on the left leg was immediaetly encased in an impervious dressing and the patient was kept constantly under the physician's surveillance thereafter. Two hours later the dressing was removed, revealing a patch identical in appearance with that on the right leg.

The entire trunk was encased in a sort of cuirasse of impervious bandages before the patient retired. On removal of the covering in the morning, lesions were found where they had previously been absent.

The patient was constantly under the watchful eyes of other patients, nurses, visitors and physicians. In one of the patients suspected of being a malingerer, not only was a strict surveillance carried out day and night, but a special nurse was employed to accompany the patient even to the toilet, and every conceivable article with which artificial lesions might be produced was kept beyond the reach of the girl.

On one occasion, a large watch crystal was applied by means of adhesive tape over a beginning erythematous patch; one of the physicians watched this patch constantly, and observed the development of the lesion as it progressed to a vesicular dermatitis.

Numerous other tests of similar character were carried out. But according to the authors, the results of these tests, convincing as they seemed to be, were in reality only negative in character. They determined to furnish positive proofs relative to the spontaneity of the eruptions.

Thus, a patient (Case 2) was observed presenting a very faintly outlined erythematous patch of skin over the region of the left kidney, of only a few minutes' duration. The lesion was watched unremittingly by a physician during the subsequent two hours. In that period of time, the patch underwent the various cyclical changes described before, terminating in a weeping dermatitis, directly under the observer's eye. When the erythema was first visible, there was absolutely no trace of epidermal changes on the surface, as would have been the case had the lesion been provoked by some artificial means.

In another patient (Case 4), the girl complained of a burning sensation over the sternum, of only a few minutes' duration. On examination, the area was found to present nothing but a faint prominence of the follicular orifices in a small spot, circular in outline. This was incessantly kept under observation, the patient stating that she felt confident that a lesion was about to develop there. A little later, the follicular orifices became markedly enlarged, a perifollicular edema supervened, followed by the usual little urticarial zone surrounding each orifice. The next phase was manifested by a serous exudation within the follicles, then an extravasation of tiny drops of blood, which ended in crust formation. There was no evidence of dermographia. At the beginning of the process, the epidermis was absolutely intact.

Many experiments were carried out to provoke lesions by artificial means, in an attempt to produce lesions simulating those exhibited by the patients. Control tests were also made. Among the methods employed were the use of a stiff-bristled nail brush, applications of ethyl chlorid, irritation by means of faradic electricity and many other irritating agents. All these experiments proved negative.

In all five patients there were associated manifestations of menstrual disorders: irregularity, scanty flow, amenorrhea, dysmenorrhea.

HISTOPATHOLOGY

For microscopic examination, the authors excised part of a necrotic lesion from the forearm. The pathologic process seemed to originate in the capillaries and deep vessels of the skin. The large and small blood vessels were greatly dilated and were surrounded by a dense round cell infiltrate. This infiltrate followed the branching vessels to their finest divisions, including the most superficial capillaries. The latter also were dilated, engorged with blood and surrounded by round cell infiltrates, some of them obliterated. These vessels were especially evident in areas underlying small epidermal vesicles. The sebaceous glands and hair follicles were surrounded by dilated and inflamed vessels; but the sebaceous and coil glands themselves were unaffected. The most pronounced changes were found about the follicles. The deeper portions were surrounded by a net of dilated and inflamed vessels; the branches of these vessels could be readily traced, with their dense perivascular infiltrates, to the subepithelial layer of the skin.

Surrounding the follicular orifices, the epidermis was raised by the exudate and under it was a layer of blood and fibrin. The little necrotic area was enclosed in a vesicle "membrane" (Blasenwall), toward which dilated vessels, surrounded by inflammatory infiltrates, were seen coursing. The small cutaneous nerves exhibited no signs of inflammation or other changes.

The histopathologic picture gives the impression that the pathologic process originates primarily in the blood vessels; the inflamed and thrombotic vessels give rise to exudation, the formation of vesicles, and eventually necrosis. It may be safely assumed that the inciting agent of the dermatosis lies in the blood vessels—an assumption favoring the so-called "hematogenous inflammatory theory."

In their concluding paragraphs, Matzenauer and Polland state:

> Our dermatosis is characterized by peculiar, spontaneous inflammatory manifestations, usually appearing symmetrically, in chronic successive crops; the lesions are partly erythematous, partly urticarial in nature, most often, however, appearing in the form of a weeping dermatitis; more rarely, as spontaneous necroses of the skin. Coincident with the disease, there are frequently vasomotor disturbances of the heart and circulatory organs, and sometimes also, psychic manifestations.

These changes appeared only in women suffering from dysmenorrhea, and are based on a constitutional affection, most probably invoked by toxic metabolic products, due to malfunction of the ovarian follicles.

REPORT OF A CASE

The patient whose history is here recorded gave a personal history and exhibited lesions that seemed to conform in almost every important detail with Matzenauer and Polland's description of dermatitis dysmenorrheica. She was presented before the New York Dermatological Society, May 25, 1920. At that time, the patient had been under our observation only a short time and the presentation was accordingly brief. Furthermore, the lesions that she exhibited on the day of the meeting were in the final stage of evolution, consisting of little more than a moderately inflamed area of yellowish skin on the left cheek, which gave the appearance of having been bruised. Following the presentation of the patient, the discussion of the members brought out the fact that the majority looked on the lesion as being of artificial character—most likely self-inflicted. After the total subsidence of the lesions then present, we had the opportunity of observing the patient for a period of time embracing two successive menstrual cycles, during which new eruptions appeared, permitting careful study of their involution and evolution.

History.—Mrs. H. B., aged 30, married, of Russian birth, referred to us by Dr. Elihu Katz of this city, a resident of Bangor, Me., complained of a recurrent eruption on the face and chest, the duration of which was one and a half years. The father was living and well, except for occasional "heart and lung trouble." The mother was living and well. Three brothers were dead; the first and second brothers were born before her, the first was possibly still-born, and the second lived two days after birth; the third, two years younger than she, died of pneumonia at the age of 28. Two sisters died in infancy before she was born. One sister, six years older, now living, had "kidney and bladder trouble." Her paternal grandfather was asthmatic and had been in bed four years with "rheumatism." Her paternal grandmother had "stomach trouble." The maternal grandfather died nine years before of cancer. The maternal grandmother had been paralyzed and bedridden for four years, and had kidney disease with edema. There was, then, history of heart trouble in the father; no tuberculosis in the family; kidney trouble in the maternal grandmother; no epilepsy, insanity or nervous derangement; cancer only in the maternal grandfather and no history of skin diseases in the family.

The patient had had measles, mumps and scarlet fever in childhood and a severe attack of typhoid fever at the age of 9. Tonsillitis appeared every winter. There was no history of "rheumatism." She had had influenza-pneumonia two years before, complicated with pregnancy. She underwent an abdominal operation five years before, but did not know its nature. The left tympanic membrane had been lanced three and a half years before for otitis media. She had been married eleven years; her husband was living and well. She had had four children; the first two were living and well, the third was still-born at 7 months, the fourth died of pneumonia at 8 weeks. The last pregnancy was in the winter of 1919.

She had had frequent supra-orbital headaches, of migrainous type, associated with attacks of vomiting, during the last nine years. Eye-glasses fitted by a physician did not help these headaches. She had had frequent tinnitus in the left ear since the attack of influenza. There was no muscae volitantes. There was no history of "nervousness," poor memory, hysteria, etc. She heard well with both ears, but had an intermittent left aural discharge since the attack of otitis. There was no history of trouble with vision, but on account of headaches, she had glasses fitted nine years before. There was no history of epistaxis until the headaches began; since when it had occasionally accompanied the headaches, never being profuse and being always easily stopped. The teeth had been good until the first child was born; they had ached often since, and several had been extracted; a few had been filled. She had pyorrhea; there was no history of sore mouth, nor of diphtheria. Until two years before, she had had recurrent herpes labialis at the angles of the mouth. There was no history of nasal discharge, catarrh or nasal operations. Colds were frequent, with coughing and rhinitis, but she had had none recently. She had had "weak lungs" seven years before, treated at the Johns Hopkins

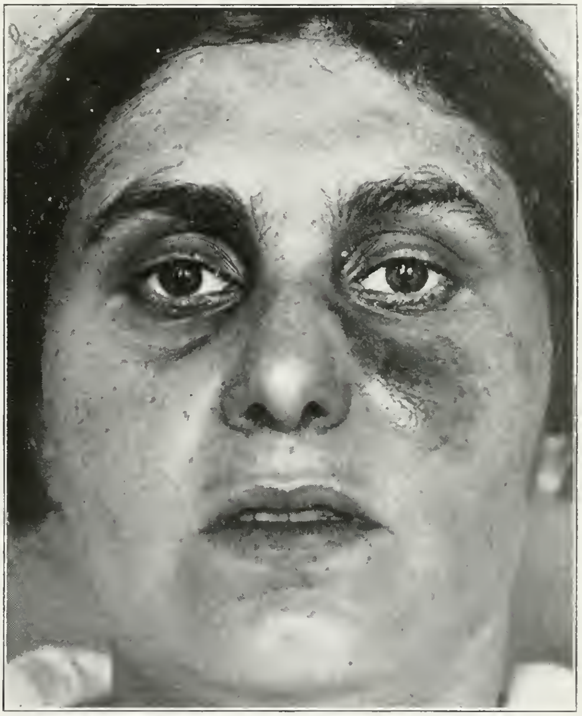

Fig. 1.—Patient on the third day of the menstrual period, showing circumscribed patch of erythema with beginning vesicle formation on the left cheek, which is spreading rapidly and is surrounded by a faint zone of erythema.

Hospital. At that time she had hemoptysis, night-sweats and an afternoon rise of temperature, together with loss of weight—from 180 to 129 pounds. She still had night sweats (?). There was no history of heart trouble. Her ankles and legs often became swollen so that she could not lace her shoes nor walk. She slept comfortably on one pillow; there was no dyspnea nor orthopnea. Her heart palpitated and she felt short of breath when she climbed a few stairs. She had had palpitation and shortness of breath for the last seven years. Her appetite had always been good, until she had influenza two years before, since which time it had often been poor. There had been no stomach trouble. She had been constipated frequently. There was no diarrhea, no history of hemorrhoids, nor of urinary trouble and frequency.

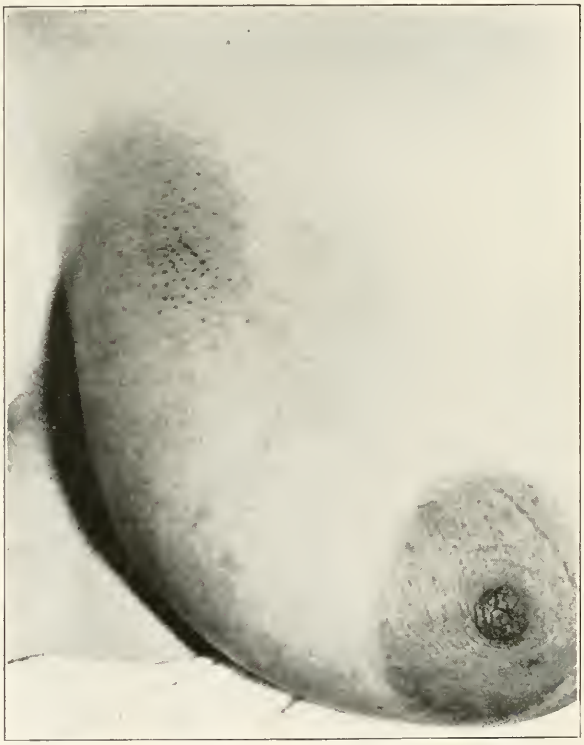

Fig. 2.—Condition on the third day of menstrual period, showing dollar sized area of follicular petechiae on the left breast near the sternum, accompanied by slight erythema. The patch is spreading.

Menstruation began at the age of 12, and the second period occurred six months later. After that, it occurred regularly every twenty-eight days, lasting six or seven days and was quite profuse, associated with cramps which at times were severe. This kept up until her marriage eleven years before, since when she had menstruated every three weeks, and often twice a month, the periods being irregular. There were severe backaches at each period, and cramps the same as before her marriage. There had been a very scanty flow for the last four or five years, lasting four or five days each time, with a white discharge at times between the periods.

There had been no history of joint pains until the last four years, since when she had had occasional pains in the ankles, often so severe that she could not touch the parts. There was no history of any accidents or fractured bones. Seven years before, she had a yellow, weeping, vesicular patch on the skin of the left calf, which appeared independently of her menstrual period.

Present Illness.—One and a half years before, at the time of the menstrual period, she noticed a burning sensation under the left eye. A little red spot, followed by blister formation, appeared, later becoming covered with a yellow crust. The same phenomenon had accompanied each menstrual period since then. The patch had increased in size each time, until it now occupied the entire left cheek and part of the left side of the nose. Four months before she first noticed a similar spot over the skin of the lower sternum; this likewise appeared with each period and at no other time, and increased in size each time, until it extended over part of the left breast including its lower quadrant. During the period of gestation, in the winter of 1919, there was an entire absence of the eruption. The burning sensation preceded the appearance of all the efflorescences.

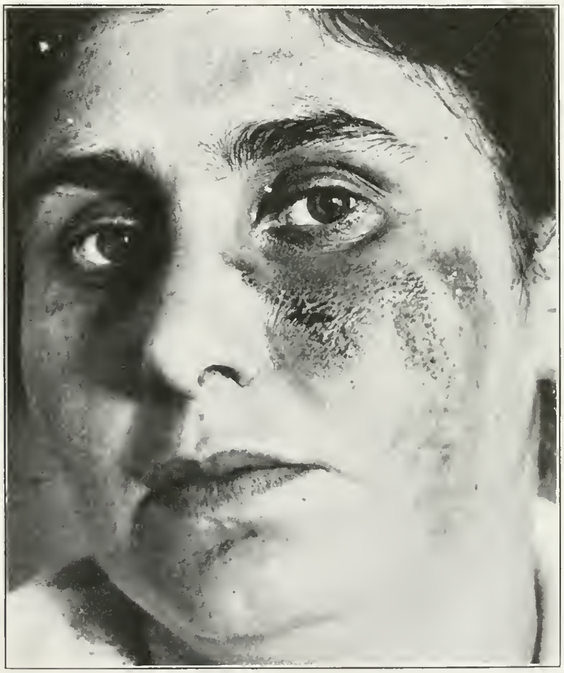

Fig. 3.—Patient on fifth day of the menstrual period, showing involvement of the entire cheek; erythema, edema, follicular hemorrhages and blood crusts, with remnants of small vesicles. The patch resembles an ordinary recent bruise.

Physical Examination.—The patient was a well developed, well nourished, somewhat adipose woman of 30 years, able to be about daily, and apparently in good spirits. She was fairly intelligent, and cooperated fairly well with the examiner. The skin was of good color, of normal moisture and texture, with a rather liberal supply of subcutaneous fat. On the abdomen were multiple lineae albicantes. In the left hypochondrium appeared a flat, depressed soft, pitted, depigmented scar, as large as a 50 cent piece, the origin of which was unknown.

The lesions which directly concern us occupied the left cheek and the midsternal region, with an extension involving the left breast. They appeared as diffuse, brownish-red patches, irregular in size and outline, with a few remnants of brown crusts; the follicles in these areas appeared as darkbrown punctae.

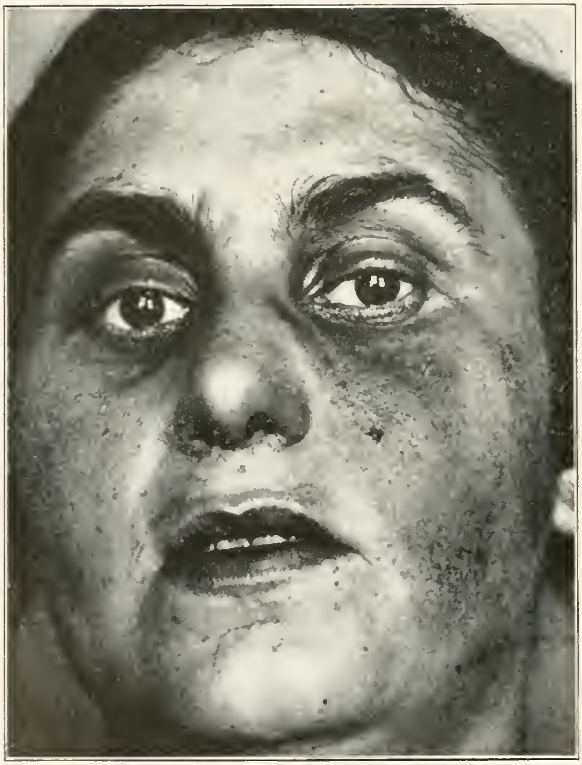

Fig. 4.—Patient on eighth day of menstrual period, showing the lesion on the left cheek in the final stages of evolution. The left cheek is somewhat edematous, yellowish and shows scattered, small adherent blood crusts located in the follicular orifices.

The corneal and pharyngeal reflexes were active. The thyroid gland was normal in size and shape. Examination of the heart and circulatory system proved negative; but auscultation in the second intercostal space, just to the right of the sternum, revealed a slightly tympanitic quality in the note of the second (aortic) sound; this was not transmitted elsewhere. Abdominal visceral examination was negative

There was a little superficial hyperesthesia on the anterior surface of the left leg and thigh; there was no disturbance of temperature sense in this area. There were varicose veins. No edema or cyanosis was present. The reflexes were normal throughout. The gynecologic examination made by Dr. Combes, Jr., proved negative, with the exception of the presence of a slight cervical tear.

Blood count, June 16, 1920, revealed: white blood cells, 11,400; red blood cells, 4,476 000; hemoglobin, 75 per cent.; polymorphonuclear leukocytes, 68 per cent.; small mononuclears, 24 per cent., and large mononuclears, 8 per cent.

Urine examination revealed: acid reaction; specific gravity, 1.013; no albumin, sugar or casts.

The blood Wassermann reaction was negative. A spinal puncture was not made.

Unfortunately, the patient refused to submit to a biopsy.

Neurologic Examination.—We are indebted to Dr. Louis Casamajor for these reports:

"NEUROLOGICAL DEPARTMENT, COLLEGE OF PHYSICIANS AND SURGEONS

"May 24, 1920

"In connection with the above case, referred to us today, examination shows no evidence of any organic nervous disease. The question of the presence of a psychoneurosis must be held open. She shows some slight signs of an anxiety type of neurosis which may be due to her skin lesion in part. I do not think it is causative."

"June 4, 1920

"I have just examined your patient, Mrs. M. B., and feel that I have little to add to the diagnosis. Besides the facial rash on the left side which she has had for the past eighteen months, for the past two months she has been complaining of a pain and weakness in the left arm and leg of an obvious neurotic character. Physical examination is quite negative, except for a general deep tenderness with superficial hypo-esthesia confined to the left side of the body, which is a typical neurotic finding.

"It is rather difficult to learn much of this person's personality. She is a dull, stolid, not to say stupid, individual, and one whose personal history it is difficult to obtain. She appears to be fairly well satisfied with her life, probably a little more so than most people. She has been married for eleven years and has borne three children, of whom two survived. She seems fairly satisfied with her husband, except for the fact that his earning capacity is low. She apparently is not a deep feeling person, with little desires of any sort, but what she has of love desires seems to be satisfied by her husband with but little effort on his part. I do not feel that there is anything psychogenic in this rash. The type of neurosis from which she suffers is a superficial one and probably has much more to do with her maladjustment in her social and financial sphere, than to anything more deeply instinctive."

Subsequent Observations.—The patient visited us for the first time, April 29, 1920, within a day or two after the termination of the menstrual period. The lesions at that time had almost completely involuted, so that nothing more than a brownish yellow patch of pigmentation was seen on the left cheek and left breast. As stated, she lived in Maine, and was then on the point of going back to her home; but the desirability of remaining here until the next menstrual period was explained to her, to enable us to observe the eruption in its earliest stages and subsequent development. To this she agreed. Thus we were enabled to note the various cyclical changes pictured in the affected areas, from the beginning to the end of two successive menstrual periods.

At her initial visit, she complained of severe pelvic "cramps." Twenty drops of benzyl benzoate, to be taken twice daily, was prescribed, to be administered as soon as the first signs of menstruation became manifest. The remedy proved efficacious in preventing the onset of the usual cramps but the eruption appeared exactly as it had before and at the same relative time.

DESCRIPTION OF THE ERUPTION

The eruption is best described by enumerating its successive stages: (1) burning or tingling, (2) erythema, (3) edema, (4) vesiculation, (5) exudation, (6) hemorrhage, (7) crust formation and (8) pigmentation.

Two or three days before the beginning of the menstrual period, the patient experienced a burning or tingling sensation in various parts of the body, most frequently on the cheeks and breasts. As soon as the menstrual flow was established, a faint red spot appeared on the left cheek, near the nose, and on the left breast, near the sternum. The opposite areas, on the right side, remained unaffected as to the eruption, but the subjective sensation continued, gradually subsiding with the progress of the menstrual cycle. In the two affected sites, the areas of erythema became slightly elevated and assumed the appearance of an ordinary urticarial wheal. This lasted from six to eight hours. Soon thereafter, the surface of the patch took on a stippled appearance—due to the prominence of the dilated follicular orifices. Up to this stage, both the facial and mammary patches underwent identical changes. Then a divergence took place. The process in the facial lesion went on to the formation of distinct, pinhead sized vesicles, filled with clear serum. These vesicles, which lasted about one day, were perifollicular in location, and, soon bursting, their remnants coalesced to form a uniform patch of what looked like an ordinary weeping dermatitis. This lasted two or three days and was followed by quite distinct, although very minute hemorrhages into the follicle mouths. The appearance then was that of an existing dermatitis which had been severely bruised subsequently, causing slight superficial hemorrhages; it looked much like the injury one sustains by falling on the pavement and scraping the skin of the face against the stones. Almost as soon as the hemorrhagic stage was reached, involution began; the lesion became crusted; the crust adhered for three or four days and gradually dropped off, leaving a somewhat reddened, edematous and pigmented area, very much like that following an ordinary bruise. This area was surrounded by a broad band of erythema.

In the breast lesion, the process seems to come to a standstill as soon as the follicular hemorrhages supervene. The final stage here (at least on the two occasions when we observed the spots on the breast) appeared to be a circumscribed area of slightly inflamed, yellowish skin, in which the follicular orifices were filled with tiny brownish plugs of dried blood (Fig. 2). This area also was surrounded by a faintly erythematous zone. Finally, resolution took place, leaving a faint, yellow pigmented spot with indistinct borders.

The duration of the active eruption varied from a week to ten days.

It is to be emphasized that at the very inception of the patches the epidermis was intact.

COMMENT

The eruption corresponds in all essential features to that described by Matzenauer and Polland. The progressive cyclical changes, beginning with burning and tingling and ending with follicular blood crusts and pigmentation, are identical. The points of divergence are the absence of symmetry and the absence of necrotic and linear lesions in our patient. Both these are unessential features, however, for the confirmation of the diagnosis of dermatitis dysmenorrheica. Some of Matzenauer and Polland's patients had eruptions which were at times unilateral, and not all of their patients had linear necrotic lesions.

Since our patient was in good health, and refused to stay in a hospital, we were unable to follow the usual procedures of stable and impervious bandaging, strict surveillance, etc., to eliminate the possibility of malingering, or the question of conscious or unconscious self-infliction. We can only state our belief, not to say conviction, grounded at least in part on experiences with true malingerers, that the lesions in this patient were entirely spontaneous.

Perhaps it is not amiss to add that the eminent neurologist who examined the patient on two occasions received the same impression.

The fact that there was an entire absence of the eruptive phenomena during her pregnancy in the winter of 1919 is worthy of reiteration.

In addition to the benzyl benzoate prescribed for the dysmenorrhea, the patient was ordered to take a preparation of endocrine extracts. To the lesion on the face, one unit (skin distance) of roentgen rays was applied, in four divided doses, at weekly intervals. Subsequently to this treatment, she returned to Maine. At the time of the next menstrual period she reported by mail that there was no recurrence of the face lesion, but that the patch on the breast (which had not been radiated) was "very bad." This vague report has not, however, been verified as yet. We venture the opinion that until a more definite account of the subsequent behavior of the eruption is obtained, the question of the effect of the radiation is not to be seriously considered. Whether or not the endocrine extracts, empirically prescribed, had any beneficial effects in a month's time, is also a matter for speculation.

FURTHER REPORTS IN THE LITERATURE

The occurrence of cutaneous eruptions associated with menstruation is, of course, quite common. In 1906, Bulkley[3] published a booklet on the subject. In this he quotes all the relevant literature up to that time. In relating the case reports in the literature, Bulkley does not attempt any separation between the ordinary "menstrual" eruptions and "dysmenorrheic" eruptions. Some of his quotations of interest in connection with dermatitis dysmenorrheica are as follows:

> Edebohls[4] has reported the case of a girl, aged 19, who presented a peculiar erythematous eruption on the right side of the face, from the middle of the temple to near the angle of the jaw. The eruption had appeared regularly two days before the menstrual flow, fading with its cessation. This had occurred for three years, from 15 to 18 years of age, with then an interruption of nine months, when it again recurred regularly each month. She suffered from severe dysmenorrhea, for which she was curetted, when the eruption ceased for three months. Double ovarian disease was then discovered, and the organs were removed, but the eruption "reappeared with clock-like regularity once a month," and rather more intensely.
>
> Laredde[5] presented at the French Dermatological Society a woman, aged 33, who for nearly twenty years had had certain eruptions recurrent at almost every menstrual period. On the face the eruption was herpetic, but on the hands there were papules and patches of erythema multiforme, and on the legs occasional purpuric lesions. (Dysmenorrhea is not mentioned.)
>
> McGillicuddy[6] records the case of a young lady, aged 20, with extremely painful menstruation, who had, with each period, swelling of the left foot and leg, and also of the face. He says, "I have seen her face much distorted on these occasions by edema around the eyes and at the base of the nose."
>
> Engelmann[7] mentions two cases in which there were small tumefactions on the forehead, breast and back, which appeared at the time of menstrual con-

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[3] Bulkley, L. D.: Influence of Menstrual Function on Certain Diseases of the Skin, New York, Rebman Company, 1906.

[4] Edebohls, G. M.: New York J. Gynec. & Obstet. **2**:55, 1892; ibid. **3**:48, 1893.

[5] Laredde: Ann. de dermat. et syph., 1899, p. 130.

[6] McGillicuddy, T. J.: Functional Disorders of the Nervous System in Women, New York, William Wood & Co., 1898, p. 77.

[7] Engelmann: The Hystero-Neuroses, Tr. Am. Gynec. Soc., 1887.

gestion, passing away with the cessation of the menstrual flow as rapidly as they had come. The patients were the subjects of uterine disease and suffered from many other reflex symptoms.

Bulkley further quotes numerous examples of menstrual eruptions, such as herpes, urticaria, angioneurotic edema and erythema multiforme, occurring in women whose menses were normal, as well as in those afflicted with dysmenorrhea and other pelvic disturbances.

None of the cases in Bulkley's booklet, however, falls into the same category as our case of dermatitis dysmenorrheica. His cases are all banal skin diseases, occurring at the time of the periods, or aggravated by the onset of menstruation.

In the *Ikonographia dermatologica* for 1909, Zieler published an interesting article entitled, "Exanthema menstruale angioneuroticum." In the case reported by him, there were also no symptoms of dysmenorrhea, but the eruption had appeared, for three and a half years, just before each menstrual period, and had vanished between the periods. The parts affected were the ears, the backs of the arms and hands, especially the fingers, the gluteal region, the sides of the legs and the backs of the feet. The eruption was of the "angioneurotic edema" type, with urticarial wheals and inflammatory nodules, associated with petechiae.

In the last two or three years, several articles on dermatitis dysmenorrheica have been published by Brauer and by Polland. Unfortunately, these are not available at present, with the exception of a brief article by Brauer. In 1917, Polland[8] published a second article entitled "Dermatitis dysmenorrheica symmetrica," and in 1919,[9] an article on "new clinical studies to clarify the differences between dermatitis dysmenorrheica, herpes neuroticus and self-inflicted dermatoses." Brauer,[10] in 1918, published an article under the presumably satirical title, "A Case of So-called Dermatitis Symmetrica Dysmenorrheica in the Male." Whereupon Polland promptly took pen in hand, attacking and criticizing Brauer's conceptions and opinions on the subject, thus rousing Brauer's ire to the point of publishing a brief but cogent reply. In this communication, Brauer[11] maintains his view that the syndrome described as an entity by Polland may be demonstrated in the male sex. He fortifies this opinion by quoting Edel,[12] who, under the title "Multiple Psychogenic Skin Defects of Inflammatory Character," described a case of dermatitis "dysmenorrheica" in a 13 year old boy. In this case it was demonstrated that "the inflammatory plaques could arise only on the basis of neurogenous manifestations."

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[8] Polland, R.: Dermatitis Symmetrica Dysmenorrheica, Arch. f. Dermat. u. Syph. **124:** (April) 1917.

[9] Polland, R.: Neue klinische Beiträge zur Klarstellung des Unterschiedes zwischen Dermatitis dysmenorrheica, Herpes neuroticus und Selbstschädigung. Dermat. Ztschr. **28:** 1919.

[10] Brauer, A.: Dermat. Ztschr. **26:** 1918.

[11] Brauer, A.: Nochmals ein Fall sogenannter Dermatitis symmetrica beim Manne, Dermat. Ztschr. **29:**211 (April) 1920.

SUMMARY AND CONCLUSIONS

Our patient presents a syndrome which corresponds in all essential details to that described by Matzenauer and Polland. She has dysmenorrhea, and each menstrual period is accompanied by a regularly recurrent, more or less characteristic eruption, manifested by edema, erythema, follicular hemorrhage, crusting, and pigmentation. The patient has a decidedly phlegmatic temperament.

Between the menstrual periods, the eruption vanishes.

During pregnancy the eruption remains in abeyance.[13]

Self-infliction, malingering, neurotic excoriations, etc., play no part whatever in the causation of the dermatosis.

The dermatosis, undoubtedly one of extreme rarity, is in all probability a disease entity.

24 West Fifty-Ninth Street.

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[12] Edel, K., quoted by Brauer: Nederlandsch. Tijdschr. v. Geneesk. **1**:1433 (May 25) 1918; abstr. Deutsch. med. Wchnschr., 1918, No. 28.

[13] Since this was written, we have been informed that the patient has been pregnant three months. During this period there have been seen no signs of the eruption.

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VARIOLIFORM ATROPHIC FOLLICULITIS

FOLLICULITIS ATROPHICANS VARIOLIFORMIS

LOUIS SAVATARD, M.D.
President Manchester Dermatological Society
MANCHESTER, ENGLAND

In May, 1918, Heidingsfeld [1] reported a case of "atrophia maculoso varioliformis cutis." In the following number of the journal MacKee and Parounagian [2] give a complete clinical and histologic record of two cases that they called "folliculitis ulerythematosa reticulata" and, in the course of the survey of the literature of these peculiar and rare conditions, refer to Heidingsfeld's case, while at the same time recognizing its difference to theirs. When I saw these cases I was under the impression that though they differed somewhat clinically, we should establish their identity histologically, for I had had two such cases, the one, identical with Heidingsfeld's, which I [3] exhibited at the Manchester Dermatological Society in 1912 and the other, the facsimilie of MacKee's, which I demonstrated in 1914. Lately I investigated the cases histologically and found that my impression was incorrect. Heidingsfeld, unfortunately, was not able to make a biopsy.

REPORT OF A CASE

History.—The case I now record was that of a young man, aged 17, who in October, 1912, presented himself at my clinic with pitted atrophic scars on both cheeks, more marked however on the left, and beginning on the latter side three-quarters of an inch below the left external canthus extended downward to the angle of the jaw (Figure 1). The scars varied in size from that of a pinhead to that of a split pea and in places two or more had coalesced, forming a furrow. In the lower part some slight capillary dilatation was evident and a few minute comedones could be detected on both cheeks. The condition was first noticed over the left malar region some four years previously, and for two years the patient had gone elsewhere for treatment, but had recently been discharged as incurable, and had been warned that the scarring would extend and eventually destroy his face. The man's hands and feet showed venous stasis with marked hyperhidrosis. Aside from the fact that his mother had been treated at the hospital some years previously for lupus vulgaris, the family history was of little interest.

The patient had not suffered from smallpox nor had had any pustular eruption of the face.

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[1] Heidingsfeld: J. Cutan. Dis. **36**:285 (May) 1918.

[2] MacKee and Parounagian: J. Cutan. Dis. **36**:339 (June) 1918.

[3] Savatard: Brit. J. Derm., (April) 1912, p. 158, and (Jan.) 1918, p. 46.

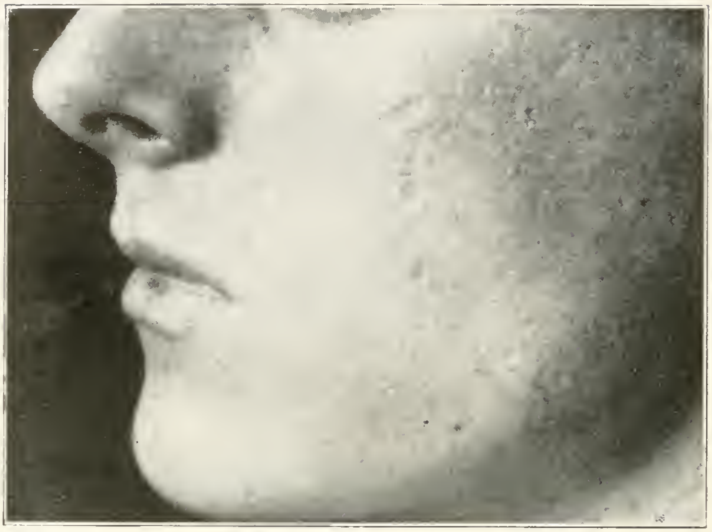

Fig. 1.—Varioliform atrophic folliculitis. The transverse furrow above was excised for histologic examination.

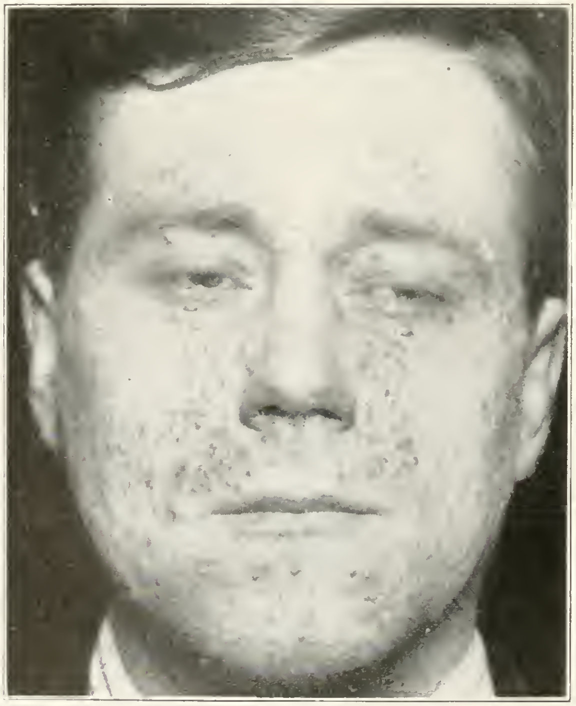

Fig. 2.—Varus nodulosus; active stage.

I have seen the patient again recently and find the condition practically in statu quo. There has been a slight increase on the right cheek and the pitting seems to be a little more pronounced. There is no evidence of telangiectasis or erythema. Careful palpation gives one the impression that at the edges of the scars the skin, though apparently normal, is slightly firmer than normal, though it does not amount to induration.

Histologic Examination.—I excised the transverse furrow for histologic examination. I found, on examination, flattening of the papillary layer with atrophy of the hair follicles, diminution of elastic tissue and increase of collagen fibers. At the margins of the atrophic area there was perivascular and perifollicular small-celled infiltration. A sweat gland was greatly distended and suggested the obliteration of its duct. There were increased vascularity and proliferation of the vessel walls. The picture was that of an atrophy secondary to chronic inflammation.

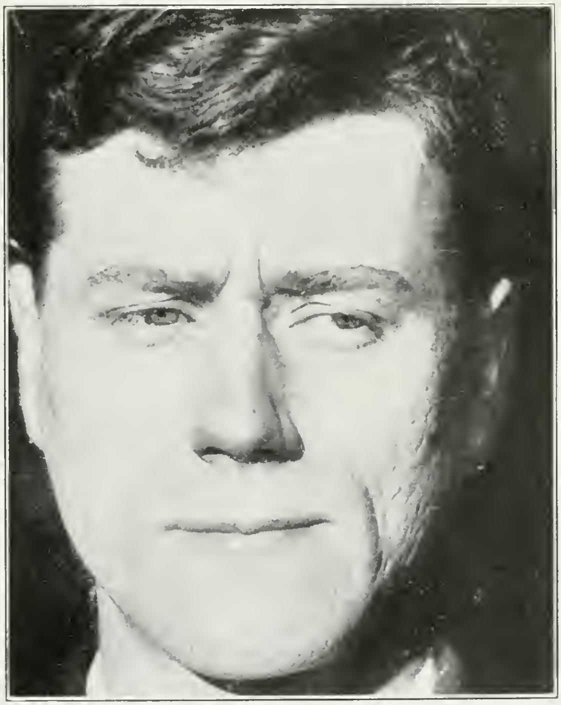

Fig. 3.—Varus nodulosus; atrophic stage.

I have preferred calling this condition varioliform atrophic folliculitis rather than adopting Heidingsfeld's title. This name not only conveys the clinical picture, but also explains its etiology.

There are, of course, many varioliform atrophic conditions of the skin from which a differential diagnosis must be made; for example, atrophy following follicular lupus, acne varioliformis, and acne agminata (Radcliffe Crocker[4]), which, however, Brooke[5] described as varus nodulosus. The atrophy in these conditions is, however, secondary to a well marked eruption. Varus nodulosus not only simulates variola in its atrophic stage, but is extremely like it in its initial outbreak, as Figures 2 and 3 show.

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[4] Crocker: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., Ed. 3, Vol. 2, p. 1096.

[5] Brooke: Ikonographia Dermatologica, 1906.

SCLERODERMA AS A POSSIBLE MANIFESTATION OF CHRONIC ARSENIC POISONING *

SAMUEL AYRES, Jr., M.D.
LOS ANGELES

In three consecutive cases of diffuse scleroderma seen at the Massachusetts General Hospital within the past six months, the urine has given positive tests for arsenic. One patient, a storekeeper, had kept powdered arsenate of lead under her counter for over four years to kill mice; another had handled glazed paper in a paper box factory for ten years; the third had been exposed to the use of insecticides about the house for a number of years, but so far as could be ascertained, this occurred after the onset of the scleroderma. Further investigation into the records of two other patients, who had died, showed that they had probably been exposed to arsenic. All five of these cases were examples of diffuse scleroderma with brown pigmentation, and the condition of the three patients whom I saw personally and whose urine was positive for arsenic began with sclerodactylia, that being at present the most noticeable and most annoying symptom. Letters were sent to all former patients with undisputed scleroderma of whom we have records, nine in all, but no replies have been received.

Only one case of localized scleroderma or morphea has been studied from this angle. The patient, E. M. (O. P. D. 416812), a young woman in her twenties, had for many years been exposed to arsenic in the form of arsenical sprays in a large garden at home and in her capacity as director of school gardens. Within the past six months there had developed a saber-like, white, depressed firm lesion in the middle of the forehead extending from above the hair line, ending in a point just above the bridge of the nose, and surrounded by pale brown pigmentation. There were no subjective or constitutional symptoms. The urine gave a positive test for arsenic.

Were it not for the fact that scleroderma is such a rare disease, this paper would not be offered for publication until more cases could be analyzed; but it seems desirable to make public the facts so that they may be corroborated or refuted by as many observations as possible. It is not intended here, to urge a connection between scleroderma and arsenic poisoning, but merely to point out the possibility. The original suggestion was offered by Dr. William H. Smith of this hospital in the discussion of Case 1.

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* From the Department of Dermatology, Massachusetts General Hospital, Boston.

REPORT OF CASES

CASE 1.—*History.*—West Medical 235661. H. E., a man, aged 35, a native of Massachusetts, whose family and past history were unimportant, had been a foreman in a paper box factory for ten years, having come in contact with such materials as glazed paper, cardboard, much paper dust, dextrin, hoof glue and flour paste.

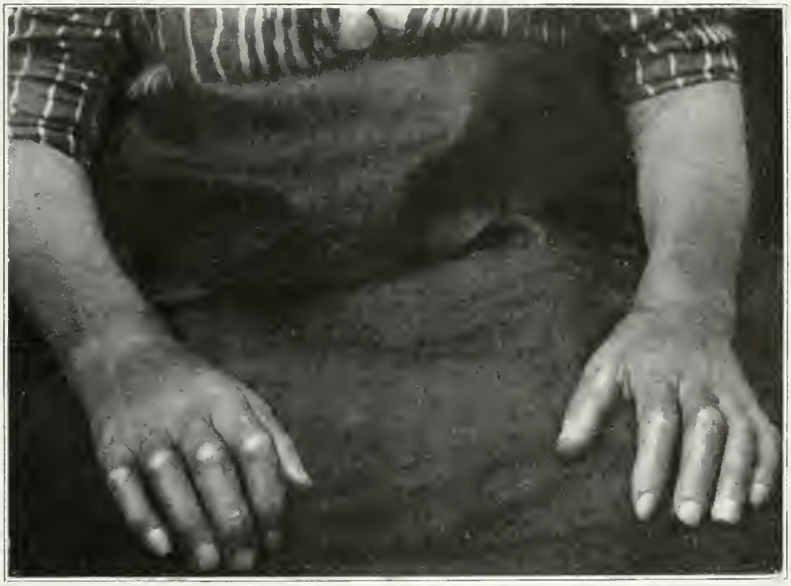
The present illness began one year ago when he noticed that his right hand was weak and that bowling balls slipped out of his fingers. His hands were slightly stiff and the palms a little sore. The soles of his feet were also somewhat sore; he was treated by his local doctor for fallen arches without receiving much relief. After about a month of these mild symptoms he felt comparatively well except for slight soreness of the palms and soles. Six months before entrance into the hospital he noticed that his symptoms were becoming gradually worse. The soreness and stiffness increased; his hands were frequently swollen in the mornings, and they perspired a great deal; at times they were painful on pressure or contact. On exposure to cold the fingers ached and became white or dusky. At present all of his joints are stiff after inactivity, but the fingers are constantly stiff in a position of slight flexion and are capable of little mobility. He had always slept well until about a month ago; since that time he has been restless at night and has slept poorly. He has lost about five pounds during the past year. For the past three months he has taken three pills daily, prescribed by his doctor for "rheumatism." There has been no soreness of the eyes, tongue or throat, and no gastro-intestinal disturbance.

Physical Examination.—This revealed typical sclerodermatous changes with diffuse brown pigmentation involving the hands, forearms, chest and abdomen; the palms were wet with perspiration. The only other positive findings were: a slightly irregular left pupil, enlarged epitrochlear and cervical lymph glands and systolic murmur at the cardiac apex transmitted to the axilla. The blood pressure was systolic 120, diastolic 64. Temperature and respirations were normal. The pulse rate varied between 68 and 85. When seen five months later, there were no changes except for the presence of numerous small keratoses on the backs of both hands.

Laboratory Examination.—The results of the laboratory examination were: urine, no albumin, sugar or sediment on two examinations; renal function, 45 per cent. phenolsulphonephthalein in two hours and ten minutes (normal). The blood smear was normal on two examinations. The white blood count was 8,400; hemoglobin (Talqvist), 80. The routine stool examination was negative. The blood Wassermann reaction was negative. Blood uric acid was 4.1 mg. per 100 c.c. (high). Roentgen-ray examination of the hands and wrists was negative; it showed that the heart was slightly longer than normal. The basal metabolism was 10 (within normal limits). Analyses of the urine and stool for lead and of the stool for arsenic were negative; analysis of the urine for arsenic was positive. Analysis of specimens of four kinds of paper used in the factory, showed arsenic to be present in three—a rough finish gray paper, a tan paper, and a brown cardboard; no arsenic was found in a sample of white glazed paper.

CASE 2.—*History.*—Skin 226621. L. R., a woman, aged 40, born in Russia, lived in Massachusetts for twenty-two years. Her family and past history were unimportant. For the past eight years she has kept a small grocery store in a damp basement. For over four years it had been her habit to keep an open saucer filled with powdered arsenate of lead under her counter for the purpose of killing mice.

The present illness began about four years ago with numbness, coldness, cyanosis and pallor of the finger tips of both hands. After persisting rather constantly for two years the fingers and hands gradually became stiff and brown. For the past two years there has been a constant aching pain in the hands and fingers, and the stiffness has progressed to practical fixation. During these four years she has been troubled a great deal with pyrosis and eructations without definite relation to meals, relieved somewhat by drinking milk but not by soda; there has been no nausea or vomiting. She never had stomach trouble before her present illness. She has lost 30 pounds in the past two years and feels weak and tired all the time. Recently her catamenia has become slightly irregular and less frequent. Hoarseness has been progressive for many months.



Case 2.—Typical sclerodactylia with pigmentation, infiltration and glossy skin. Similar changes involved face and neck. The same condition appeared in Cases 1 and 3. (Photograph by Miss Harriet Williams.)

Physical Examination.—This was negative except for typical sclerodermatous changes with diffuse brown pigmentation involving hands, forearms and face. Over both elbows, where the skin seemed firmly attached to underlying structures, a coarse crepitation was heard and felt on motion, a phenomenon not noted elsewhere. Blood pressure was systolic 112, diastolic 70. Temperature, pulse and respiration were normal.

Laboratory Examination.—One routine urine examination was negative. The blood smear was normal. The white count was 14,000 (one estimation), hemoglobin 90 (Talqvist). A Wassermann test and stool examination were not made.

A barium roentgen-ray examination of the gastro-intestinal tract was negative. A urine test for arsenic showed that a considerable amount of arsenic was present.

Case 3.—*History.*—East Medical 229709. L. R. S., a woman, aged 24, who had always been a resident of Massachusetts, had a negative family history. Her past history showed measles and mumps in childhood, peritonsillar abscess nine years ago which was incised, and pneumonia two years ago. Careful questioning failed to elicit any exposure to arsenic, except possibly through the use of insecticides about the house.

Her present illness began about twelve or thirteen years ago with swelling of the feet and ankles without redness, but with such tenderness that she was forced to give up her work in a shoe factory where she put laces into freshly lined shoes. Some weeks or months later her hands became numb, very brown and so stiff that she was unable to bend her fingers. About five years after the onset areas of brown pigmentation began to appear about the waist, neck, chest and in the joint flexures. About two weeks following pneumonia three years ago she had severe neuritis in both arms lasting several weeks. During the past year or more the numbness and stiffness of the fingers has diminished, and the legs, which several years ago were firm and hard, are now practically normal. She thinks she has lost some weight. She sleeps well. There has been no disturbances of digestion or of menstruation.

Physical Examination.—This revealed marked pyorrhea, bilateral tear of cervix, soft systolic cardiac murmur at apex, smooth and atrophic appearance of tongue on front and sides, dry and scant hair of scalp, axillae and pubes. The skin about the mouth was wrinkled and atrophic, and on the hands and forearms it was glossy, atrophic and firmly bound down. The pigmentation apparently had faded, but was still quite well marked on the hands, forearms, neck, chest, breasts, about the waist and mouth and in the axillae and cubital spaces; on the hands and arms there were areas of depigmentation. The fingers were in partial fixation. Blood pressure was systolic 140, diastolic 80. Temperature and respiration were normal. The pulse varied between 85 and 100.

Laboratory Examination.—Routine urine examination was negative twice except that many white blood cells were present. Renal function was normal with 50 per cent. phenolsulphonephthalein in two hours and ten minutes. Routine stool examination was negative. A Wassermann test was not made. The blood smear was normal; white count 7,000; hemoglobin 80. Blood nonprotein nitrogen was 32 mg. (normal); blood phosphates, 7.8 mg. (normal); blood carbon dioxid 34.5 mm. of mercury (normal). Sugar tolerance test of the blood was normal. Urine test for arsenic was positive. The insecticide in use during the past year was negative for arsenic.

ETIOLOGY

The cause of scleroderma is unknown.[1] A number of investigators[2] believe it is caused by functional or organic disturbances of the glands of internal secretion, especially the thyroid, asserting that a certain degree of improvement followed the feeding of thyroid substance.

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[1] Stelwagon, H. W.: Diseases of the Skin, Ed. 8, Philadelphia, W. B. Saunders Company.

[2] Foerster, O. H.: J. Cutan. Dis. **34**:1, 1916.

Glandular pathology or dysfunction has not been a constant finding, and thyroid therapy has resulted in many disappointments. A basal metabolism of +10 in Case 1, however, does not suggest either a thyroid deficiency or a hyperactivity as we understand it at present. A trophoneurosis is difficult to rule out. Vascular changes in the skin which frequently occur, sometimes progressing to occlusion, are probably secondary rather than causative. A review of the literature during the past twenty years and of all the available textbooks on dermatology has failed to reveal a single statement regarding scleroderma as a possible manifestation of chronic arsenic poisoning.

ARSENIC IN THE URINE

Arsenic may be found in the urine from three to nine months after exposure has ceased. The tests in the cases reported above were made by the Sanger method in the laboratory of Dr. W. Denis of this hospital. The estimations were purely qualitative.

It may be asked how many people, or at least people without arsenic poisoning, will show arsenic in the urine. J. J. Putnam,[3] in 1890, showed that arsenic was present in traces in twenty-one of forty-eight specimens of urine selected from patients in the outpatient department of this hospital who showed no symptoms referable to arsenic poisoning. He concluded from this that the discovery of arsenic in the urine cannot be taken as conclusive proof, or even as strong evidence, taken by itself, as to the origin of doubtful symptoms. On the other hand, "notwithstanding the diagnostic value of a urine analysis in suspected cases, it is not to be forgotten that a failure to find arsenic in this way is not a positive proof that it is not in the body, since, as Taylor and others have shown, arsenic may be excreted only intermittently by the kidneys, and even in acute fatal cases, the urine has been found free."

In this hospital records of chemical tests done on various body fluids and secretions have been kept during the last four and one-half years. Arsenic was recorded as present in twelve out of a total of twenty-five tests of the urine, and in these cases, unlike Putnam's series, the presence of arsenic was suspected as a cause for the symptoms in question.

Using these two series as controls, it is seen that arsenic was found in 43 per cent. of forty-eight specimens of urine selected at random, and in 48 per cent. of 25 specimens suspected of containing arsenic. If arsenic were found in a considerably higher percentage of a large series of specimens of urine from scleroderma patients, we would be justified in suspecting arsenic as an etiologic factor—provided we could show that the patients had not received arsenical medication in the treatment of their disease. As nearly as could be det mined by direct questions and by examination of our records, n of the three patients in the cases reported had received arsenic as treatment for scleroderma, but obviously the possibility of having received it in medicine prior to coming under our observation could not be excluded.

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[3] Putnam, J. J.: Boston M. & S. J. **122**:421, 1890.

SOURCES OF ARSENIC POISONING

About thirty or forty years ago there was an active interest in arsenic poisoning because of its rather frequent occurrence from the widespread and rather careless use of arsenic in various trades and articles of common use. At that time arsenical wall paper was a common source of danger. Public health legislation has no doubt offered considerable protection, yet the danger has not been entirely removed. The following is a list of articles and industries in which arsenic is or has been used:[4] wall paper (red, orange, brown, gray, green); glazed paper and playing cards; rugs and carpets; printed or woven fabrics for use as garments, draperies, etc.; furs; artificial flowers and leaves; oil paint; lithographer's color printing; Venetian and other blinds; linoleum; japanned goods; book cloth and fancy bindings; tinted walls, bronzing, colored soaps, candy, wafers; children's toys, painted rubber dolls, rocking horses, hollow glass balls, etc.; wax ornaments for Christmas trees; anilin dyes; gloves, stockings, handkerchiefs and other articles colored by anilin; tanning hides or curing furs; smelting lead and copper; shot making; scraping paint off ships; tin plate works; galvanizing trades; electroplating; enameling; manufacture of cut glass; candles; artificial leather; hat linings; soaking of silk cocoons; glucose; beer; medicines, Fowler's solution, etc.; "sheep dip" and other insecticides for spraying gardens[5] or for household use.

One might ask how chronic arsenic poisoning could result from association with wall paper colored with arsenical dyes. B. Gosio[6] and others have shown that at least seven species of molds are capable of producing a highly toxic gas, arsin, from minute amounts of arsenical compounds in their culture mediums. This principle is applied in one of the most delicate tests for arsenic, the biologic test.[7] Penicillium brevicaule, the most important in this group of molds, has been cultivated from the air. It grows readily on decaying paper, bread crumbs, and other substances.

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[4] 4. Proc. Med. Soc. London, 1880. Oliver, Thomas: Dangerous Trades, New York, E. P. Dutton & Co., 1902, p. 378.

[5] 5. Ayres, Samuel, Jr.: Chronic Arsenic Poisoning on a Farm: Report of a Case, J. A. M. A. **71**:2122 (Dec. 28) 1918.

[6] 6. Gosio, B.: Riv. d'ig. e san. pub., 1892, p. 201.

[7] 7. Autenreith and Warren: The Detection of Poisons and Powerful Drugs, Philadelphia, P. Blakiston's Son & Co., 1915, p. 235.

People vary markedly in their idiosyncrasy to arsenic; some are poisoned readily, others are very resistant. Arsenical preparations vary in their toxicity, arsphenamin in reasonable amounts ordinarily being nontoxic, arsin gas highly poisonous, with many gradations between. According to Putnam,[3] "there is nothing more striking in the clinical history of this matter than the fact that a person who once has been poisoned, or who is naturally susceptible, is sometimes affected by exposures that seem absurdly insignificant."

SYMPTOMS

Although localized scleroderma, morphea, may be symptomless except for the objective appearance, generalized scleroderma, of which the three cases reported are examples, nearly always presents constitutional disturbances of varying type and degree. Sir William Osler [8] describes eight cases, some with severe constitutional symptoms. Herman Goodman [9] reviews sixteen cases from the literature. There is a triad of symptoms which is almost invariably present both in diffuse scleroderma and in chronic arsenic poisoning: (1) neuritic manifestations, numbness, tingling, soreness; (2) pigmentation; (3) changes in the skin itself which, however, vary in the two diseases. The comparative symptomatology of the two diseases is given in the table.

A logical and reasonable question may be raised. If scleroderma is a manifestation of chronic arsenic poisoning, why has it never been described as occurring among arsenic workers, or in persons known to have arsenic poisoning? The following facts may account for a failure to connect the two processes: (1) the extreme rarity of both diseases, especially scleroderma; (2) inadequate history in regard to exposure to arsenic in cases of scleroderma; (3) owing to the fact that the average practitioner knows little or nothing of scleroderma, the disease no doubt is often unrecognized; (4) the possibility that scleroderma may be a specialized manifestation of chronic arsenic poisoning and occur independently of other symptoms, just as tabes dorsalis may occur without any concomitant skin lesions and even without the history of infection, and just as the gastro-intestinal symptoms may be the only evidence of pellagra, or lupus vulgaris the only evidence of tuberculous infection. As a matter of fact, in Osler's Case 8, if the sclerodermatous changes could have been erased and a history of exposure to arsenic substituted, from his description of

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8. Osler, W.: J. Cutan. Dis. **16**:51, 1898.

9. Goodman, H.: J. Cutan. Dis. **38**:210, 1918.

Comparative Symptomatology of Diffuse Scleroderma and Chronic Arsenic Poisoning

Symptoms	Diffuse Scleroderma	Chronic Arsenic Poisoning
Neuritic symptoms	Numbness, tingling, aching, sometimes soreness and severe neuritic pains in involved areas, frequent multiple joint stiffness	Similar symptoms; marked cutaneous hyperesthesia
Pigmentation	Invariable, sooner or later; most marked on sclerodermatous areas; may be diffuse. May be mottled (Osler's Case 8)	Common; diffuse or localized, especially on exposed parts or in folds of joints; frequently mottled
Cutaneous changes	Sometimes erythema and edema early (edema of eyelids, Osler's Case 6); later skin becomes hard, bound down, glossy; sometimes ulceration; roughness of nails, loss of hair, hyperhidrosis of palms and soles; keratoses, author's Case 1	Sometimes erythema, frequently keratosis, diffuse or localized to palms and soles, sometimes with desquamation; sometimes papules, pustules, vesicles, or bullae; frequently edema of eyelids, roughness of nails, loss of hair; hyperhidrosis of palms and soles
Loss of weight	Usually marked	Present
Areas of involvement	Frequently extremities and face......	Motor and sensory symptoms alike affect principally the distal portions of extremities, rarely extending above elbows and knees; face frequently involved
Gastro-intestinal	Sometimes pyrosis, constipation, diarrhea, vomiting, abdominal cramps (Osler's Cases 1, 3 and 8); may be no symptoms	Same symptoms are common
Fever	Not constant; there may be several degrees during active progression of disease or at death	At times slight irregular fever
Onset	Frequently with numbness and tingling of hands and feet; sometimes with stiffness of joints; occasionally with symptoms of Raynaud's disease	Frequently with gastralgia or with numbness or tingling of hands and feet
Vasomotor disturbances	Usually present, especially in fingers; vasomotor paresis in Osler's Case 7	Common
Heart	Occasionally irregular or rapid (Osler's Case 7)	Occasionally irregular
Eyes	Not usually affected..................	Frequent conjunctivitis
Muscular weakness	Frequently present as in our Case 2 and Osler's Case 7	Ususally present
Headache	Not usually complained of...........	Common
Mouth and throat	Disease sometimes begins with an attack of sore throat; occasionally hoarseness is present	Frequent sore tongue and mouth; occasional hoarseness and bronchitis, coryza, cough
Salivation	Not recorded	Frequent; marked thirst
Anemia	Occasional	Occasional
Menstruation	Occasionally irregular	Occasionally irregular
Paralysis	Not recorded; disability from fixation	Occasional
Sudden death	Occasional (Osler's Case 7)..........	Not recorded

the case, we should have had a fair picture of chronic arsenic poisoning: weakness, marked loss of weight and appetite, gastro-intestinal disturbances, an intense bronze pigmentation, mottled in character, involving chiefly the face, thorax, abdomen and thighs.

Putnam[10] says that "lead, arsenic, and similar poisons do not always accumulate in the same organ of the body . . . but the position of greater accumulation varies according to the rapidity of absorption (solubility) of the special preparation ingested, the rapidity of elimination and similar factors." At the first opportunity a chemical examination should be made of sclerodermatous tissue at necropsy to determine the presence or absence of arsenic.

Concerning pigmentation in scleroderma, Osler[11] remarks that "there may be the muddy brown discoloration which is common in atrophic areas, or there may be a curious mottled or freckled appearance such as we so often see in the arsenical pigmentation about the abdomen. But the most remarkable instances are those in which the entire skin becomes of a deep brownish black like the most extreme form of Addison's disease." He adds that there are frequently accompanying areas of leukoderma.

PATHOLOGY AND TREATMENT

I shall not go into detail on these subjects, as they are adequately dealt with in numerous textbooks. Dinkler[12] and La Grange[13] have shown that nerve centers, peripheral nerves, heart and large vessels are free from pathologic changes. Unna[14] points out that hypertrophy of preexisting collagenous bundles is the main process, and that whatever vascular occlusion occurs is secondary to this, otherwise "we would see at a certain stage, sclerotic vessels running in normal cutaneous tissue, which we do not;" atrophy of muscles and bones, atrophy or hypertrophy of the thyroid, and atrophy of the suprarenal gland, are some of the rather inconstant necropsy findings.[1]

No successful treatment has been found. In some cases the disease undergoes spontaneous involution, in other cases it becomes arrested, and in others death occurs suddenly or after a prolonged and incapacitating illness. Massage and baking are palliative. Quartz light therapy is a suggestion.

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10. Putnam, J. J.: Boston M. & S. J. **119**:2, 1888.

11. Osler and McCrae: Modern Medicine **4**: 1915.

12. Dinkler: Scleroderma, Heidelberg, 1891.

13. Lagrange: Contribution to the Study of Scleroderma with Arthropathia, Thesis, Paris, 1874.

14. Unna: The Histopathology of the Disease of the Skin, New York, Macmillan Co., 1896, p. 1110.

SUMMARY

1. Three consecutive patients with diffuse scleroderma at the Massachusetts General Hospital showed arsenic in the urine, and two of them gave a history of exposure to arsenic. One patient with morphea frontalis had been exposed to arsenic and showed arsenic in the urine.

2. The possibility of scleroderma being a manifestation of chronic arsenic poisoning cannot be affirmed from the evidence at hand.

3. Careful histories as to the possible exposure to arsenic, a detailed record of general symptomatology and arsenic tests of the urine of a large series of cases of scleroderma would tend to determine whether arsenic plays a rôle in the etiology of scleroderma.

4. Arsenic has been found in traces in 43 per cent. of a series of forty-eight specimens of urine selected at random. It would have to be present in a much higher percentage in urine from sclerodermatous patients to be of any significance.

5. Scleroderma and chronic arsenic poisoning possess many symptoms in common in individual cases, such as neuritic manifestations, pigmentation, cutaneous alterations of various kinds, loss of weight with muscular weakness, intermittent irregular fever, gastro-intestinal disturbances, vasomotor instability, rapid and irregular heart, menstrual disturbances, etc. On the other hand, many of these symptoms may be lacking in cases of well advanced scleroderma.[15]

I wish to thank Dr. William H. Smith of the West Medical Service, Dr. David L. Edsall of the East Medical Service, and Dr. Harvey P. Towle of the Dermatological Service for reviewing and criticizing this paper. I also wish to thank Dr. William H. Smith and Dr. E. Lawrence Oliver for permission to report Case 1, in which the patient was a private patient.

820 Baker-Detwiler Building.

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[15] In addition to the references already given, the following may be of interest:

Brooke, H. G., and Roberts, Leslie: The Action of Aresenic on the Skin as Observed in the Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Derm. **13**:121, 1901.

Obituary

ISADORE DYER, M.D., 1865-1920

Another eminent American dermatologist, Dr. Isadore Dyer, died suddenly early in the morning of October 12. He had suffered from angina pectoris for two years. On October 11, he saw patients as usual during the afternoon, and went home apparently in his usual good spirits. While his death comes as a shock to the entire profession, of which he was a well-known and distinguished member, it is particularly felt by a large circle of friends in various parts of the country who recall with pleasure his genial smile and his cordial greeting.

Isadore Dyer was born in Galveston, Texas, Nov. 2, 1865. He was educated in Virginia, graduating from the Bellevue High School in 1884. He received the degree of Ph.B. from Yale in 1887. He attended the University of Virginia in 1887-1888 and received his M.D. degree from Tulane University in 1889. He was an intern in the New York Skin and Cancer Hospital from 1890 to 1892, and began the practice of medicine in Galveston. He moved to New Orleans in 1892 where he acted as professor of diseases of the skin in the New Orleans Polyclinic from 1893 to 1908. He was associate professor of diseases of the skin of the Tulane University of Louisiana, School of Medicine, from 1905 to 1908, and since 1908 professor of diseases of the skin. In 1907 he became associate dean and since 1908 has acted as dean of the medical school. He was president of the Louisiana State Medical Society, 1902-1903; of the Southern Medical Association, 1910-1911; of the American Dermatological Association, 1912-1913; of the Association of American Medical Colleges, 1915-1916; and he was a member of various social organizations. He was editor of the *New Orleans Medical and Surgical Journal* since 1896, and later editor of the *American Journal of Tropical Diseases and Preventive Medicine.*

He was appointed a first lieutenant in the Medical Reserve Corps in 1908, and served on the Mexican border in 1916. He was promoted to the rank of major when the United States entered the World War, and served on the staff of Surgeon-General Gorgas. After the war he was promoted to colonel in the Medical Reserve Corps.

For many years he was a member of the Council of Medical Education and was recently elected vice president of the American Medical Association for the second time.

He left a wife, Mercedes Percival, and five children.

Few dermatologists have contributed more articles or written on a greater variety of subjects pertaining to this special branch of medicine than did Dr. Dyer during the thirty years of his active work. His study of leprosy in connection with the Louisiana Leper Home made him a recognized authority on the subject, and his addresses on governmental regulation of leprosy, prostitution and other questions of public health, brought him prominently before the laity and gave him a world wide reputation.

G. H. F.

Abstracts from Current Literature

SUR UNE NOUVELLE DERMATÔSE D'ORGINE FILARIENNE. OBSERVEE SUR LES CONTINGENTS NOIRS (GALE FILARIENNE) (A NEW DERMATOSIS OF FILARIAL ORIGIN OBSERVED IN THE NEGRO). J. Montpellier and A. Lacroix, Presse méd. **28**:607 (Sept.) 1920.

The authors describe a papulo-pustular pruriginous dermatosis which is encountered among the Africans and is called "gale ecthymateuse." They find that the disease is due to the embryoes of the *Onchocerca volvulus.*

There is at first a diffuse modification of the skin with exaggeration of the lines giving it a shagreen appearance. This "état chagriné" is present on the trunk but is especially marked on the buttocks and the lumbar region where the thickening often constitutes a veritable pachydermia. Besides this, there is also frequently present a sort of unpolished aspect to the skin which the authors call the "état pencé." This is especially marked on the external surfaces of the arms and legs and over the knees. The skin is finely squamous, the normal lines are effaced, and thickened patches are formed which are analogous to old patches of circumscribed neurodermatitis.

Disseminated over these general diffuse changes are the eruptive elements of the disease varying in size from a millet seed to 50 centimes. The smallest of these are flat, smooth, scarcely marked, glistening papules, not so plentiful on the extremities but abundant on the trunk. Some of these papules become capped by a vesicle which rapidly becomes pustular, leaving a small crust. After removal of the crust one finds a small cicatricial excavation of a grayish-salmon tint. The larger lesions are flat and papular and are covered by a grayish-yellow crust underneath which is a small drop of thick greenish-yellow pus. Occasionally some of them from which the crust has been removed by scratching form ulcerations. Later on, after healing has taken place, the crusts become brown or black, very adherent and cover a depigmented, depressed, cicatricial surface. These cicatrices, small or large and more or less umbilicated, are numerous in some cases.

Vesiculation may also arise without a papular base and is most frequently found on the backs of the hands and fingers, resembling scabies.

The disease is essentially pruriginous, and the attacks of itching are often violent at the beginning of an exacerbation of the eruption.

The general condition of the patients may be affected. Lassitude, stiffness, articular pains, slight fever and gastric disturbances, accompanied by a curious depapillation of the lingual mucosa, are observed. There is a marked eosinophilia and an enlargement of the inguinal glands.

There is also present, usually about the costal margin and iliac crests,

There are also present, usually about the costal margin and iliac crests, small hard cysts from the size of a pea to the size of an almond in which are found the male and female adults of the filarial parasite. (This manifestation of the disease has been known for a long time, and the authors only claim credit for discovery of the etiology of the skin changes described above.)

The cutaneous changes described are due to the presence of the embryos, three or four often being found in the same microscopic field. These embryos, which are never found in the blood, apparently come by way of the lymphatics from the glands and the filarial cysts. No satisfactory treatment is known.

Ketron, Baltimore.

ETUDE ANATAMO-EXPERIMENTALE SUR LE BOUTON D'ALEP (AN EXPERIMENTAL AND ANATOMIC STUDY OF THE ALEPPO BUTTON). J. Kyrle and J. Reenstierna, Acta Dermato-Venereologica **1**:9, 1920.

Two cases came under the authors' observation, and they conducted a rather extensive laboratory investigation which is described in detail, with an excellent bibliography. Their principal conclusions are:

1. In the completely developed lesions in man, especially in those that are nearly healed, we find very few or no Leishman bodies. The abundance of the parasites in the tissue depends on the age of the process.
2. Paralleling the diminution of the organisms, certain changes take place in the structure of the tissue. At first, when the lesion abounds in parasites, we find the ordinary changes of early inflammation. Then the epithelioid cells gradually appear; during this time the organisms in the tissue are becoming more sparse. Finally it has a typical lupoid structure and therewith the Leishman bodies have been completely eliminated. The divergences we find in the literature on the subject of the abundance of parasites in the lesions and also regarding the histologic structure of the "button," are explained by the difference in age and state of development at the time of examination.
3. As we have established, the "button" is readily transferable from man to apes and also to dogs. If the virus has developed in the animals, it may easily be reinoculated in several generations; we have not been able to ascertain the limit in this regard. As to their passage through the animal body, the Leishman bodies would seem thereby to be enhanced in virulence. This has the effect of shortening more and more the period of incubation of the lesions: in our experience, the lapse of time between inoculation and the development of the nodule is reduced from a few months to a few weeks. The virus cannot become generalized.
4. The histologic changes of the "button" in animals are in perfect accord with those in man. In examining systematically all the age periods of the process in animals, we have been able to draw important conclusions on the subject of the pathology of the "button" in man, its different stages of development, and so on.
5. By virtue of the results of experiments on reinoculation in animals, we venture that, in persons who have recovered from a first attack, there exists a state of hypersensitiveness, analogous to that encountered in other processes, such as syphilis and tuberculosis.

Parkhurst, New York.

LES ICTERES SYPHILITIQUES DE LA PREMIERE ENFANCE (POSSIBLE SYPHILITIC ORIGIN OF JAUNDICE AND OTHER CONDITIONS IN YOUNG CHILDREN). Germain Blechmann, Le Nourrisson **8**:145 (May) 1920.

Observing that jaundice seemed to occur more frequently in children who presented signs of syphilis, either latent or in process of evolution, Blechmann suspected there might be some causal connection. The frequency of hepatic lesions in the new-born and in nurslings affected with syphilis, and the fact that the liver of the fetus is, owing to its location, subjected to the immediate influence of maternal toxins, and is, therefore, one of the organs conserving most readily the hereditary imprint, lent weight to the supposition. He does not regard any particular type of jaundice as being especially characteristic of syphilis, but passes in review the various types occurring in infants with which syphilis could be shown by the presence of spirochetes and by the Wassermann test to be associated, either as an accidental or as an etiologic factor. While the evidence for syphilis as a direct etiologic factor in jaundice was not overwhelming, he thinks it was sufficient to justify us in considering the question open to debate. He also discusses other conditions which he believes point to syphilitic infection, such as early rachitis affecting more particularly the skull (craniotabes), the presence of palpable bilateral epitrochlear glands, the occurrence of adenoids in infants under 3 months of age, enlargement of the spleen (provided the skin reaction with tuberculin is negative), convulsions not referable to any organic disease nor symptomatic of the onset of an acute affection (the younger the infant the stronger the indication), congenital strabismus if convergent, habitual vomiting yielding to mercury lactate, and brain disease following difficult labor. He concludes, therefore, that in the presence of any of the foregoing conditions a careful inquiry should be instituted, including a systematic examination of the blood serum, the urine and the stools, and if there is any corroborating evidence of syphilis he recommends active specific treatment in the form of intravenous injections of arsenic salts, by the jugular or epicranial veins.

H. R. W., Chicago.

ZUR ENTSTEHUNG DER IMPETIGO (CAUSE OF IMPETIGO).

Ernst Flehme, Dermat. Ztschr. **31**:111, 1920.

In fifty-five cases of impetigo contagiosa investigated bacteriologically, streptococci in pure culture or mixed with staphylococci, according to the age of the lesion, were found. In every case, the organism was of the type *Streptococcus longus*. The organisms always showed hemolysis and acid formation on mannite-litmus-agar. The impetigo streptococci were pathogenic for white mice, when large doses of the sediment of bouillon cultures were injected. At the site of injection, a circumscribed purulent lesion was formed. In man, it was possible through superficial inoculation to form typical lesions of impetigo, from which the organism was recovered in pure culture. In 15 per cent. of the skins of normal persons, and in 89 per cent. of persons with impetigo, it was possible to demonstrate streptococci, which could only be differentiated from the impetigo streptococci by a stronger red tint of the mannite-litmus-agar, and weaker hemolysis. The superficial inoculation of pure cultures of streptococci recovered from normal skin likewise produced an impetigo. In addition, scarification of healthy skin, on which streptococci were demonstrable, led to the formation of impetigo.

It seems that the cause of impetigo is the attack on fertile ground of a large dose of impetigo streptococci. The normal skin appears to have a resistance to the organism. The skin of the patient with impetigo has a lessened resistance to the same organism, yet there remains some resistance. One may consider the impetigo streptococcus as a semiparasitic organism, that under certain circumstances and in certain localities, and with a diminished resistance of the skin, leads to the formation of the disease. In addition, during epidemics, there may be an increased virulence of the organism which overcomes the normal resistance of the healthy skin.

Goodman, New York.

HERPES MENSTRUALIS. P. G. Rinsema, Acta Dermato-Venereologica **1**:87, 1920.

The case described by Rinsema presented the following points:

1. It was a skin disease which was considered as herpes because grouped vesicles appeared. It could not be called zoster because it recurred, the vesicles being small, and lasting only one week. The localization was always the same (a spot on the inner surface of the right thigh, also a smaller one on the left).

2. No congenital disturbance could be connected with its etiology.

3. The herpes appeared, when the patient was not pregnant, always a few days before the menstrual flow.

4. Twice the herpetic outbreak persisted throughout an entire pregnancy, until shortly after delivery.

The author blames some circulating irritant, which always finds the same vulnerable spot, the site perhaps of a peculiarly susceptible nerve or of anatomically defective capillaries. To find the source of this irritant is the next problem.

The time of highest development of the ovarian corpus luteum coincides probably with that of the herpetic outbreak. But why should the herpes persist throughout the two pregnancies? Simply because the corpus luteum becomes the corpus luteum verum, and in the third or fourth month its constant function is taken over by the newly formed placenta. Pregnancy and menstruation produce accentuation in certain skin diseases, and in this case herpes is no exception. But why did these herpetic attacks cease during the first pregnancy, whereas they were constantly present in the two succeeding ones? The explanation is that the first pregnancy, endocrinologically, differs somewhat from its successors.

Unfortunately, experiments could not be instituted to find whether the administration of corpus luteum or placental extract would bring a herpetic attack.

Local treatment by the roentgen ray was employed, with a filter consisting of leather and 1 mm. of aluminum, and a cure was obtained.

Parkhurst, New York.

UEBER EINEN FALL VON UEBEREMPFINDLICHKEIT GEGEN QUECKSILBER UND SILBERSALVARSAN (CONCERNING A CASE OF HYPERSENSITIVENESS TO MERCURY AND SILVER-SALVARSAN). Otto Mergelsberg, Dermat. Ztschr. **31**:129, 1920.

A young man, aged 19, was treated for a syphilitic infection. Early in the course of the treatment it was demonstrated that he was hypersensitive to mercury, and the treatment was carried on with silver-arsphenamin (doses from 0.15 to 0.25). The Wassermann test was rendered negative after the fifth injection, but the courses were continued. After the ninth injection, there was an erythema of the chest and back, moderate albuminuria, and the blood picture was: polymorphonuclears, 54 per cent.; large lymphocytes, 5 per cent.; small lymphocytes, 13 per cent.; eosinophils, 22 per cent.; transitionals, 4 per cent., and mast cells, 2 per cent. The eruption spread; the mucous membranes were affected; there was diarrhea; and the patient became much emaciated. After six weeks, he had sufficiently improved to return to the dermatologic department, where further injections of silver arsphenamin were instituted.

After the sixth injection (total of 1.2) a recurrence of the earlier symptoms set in. It took about six weeks more to bring the patient to normal. He will not be treated further unless the Wassermann becomes positive again, and in the light of the experiences to date, the drug to be used will in all probability be neo-arsphenamin.

A summary of the reported reactions to silver arsphenamin is added to the report of this case.

(I hope shortly to have the opportunity of reporting some personal observations on the effect of silver-arsphenamin of German manufacture. Earlier reports in the literature have had nothing but praise for the preparation when properly administered.)

Goodman, New York.

RE CONTINUOUS TREATMENT OF SYPHILIS INSTEAD OF CHRONIC INTERMITTENT TREATMENT. Johan Almkvist, Acta Dermato-Venereologica **1**:97, 1920.

A brief review is given of the methods of antisyphilitic treatment since the sixteenth century. With the idea that the virulence of the spirochetes may rally during the intervals of the customary intermittent treatment, the author suggests the following principles for the treatment of more recent syphilis:

1. The treatment should be continuous, not intermittent, and of great intensity.
2. From the start the treatment should be under serologic control. The sooner the Wassermann reaction disappears and remains absent, the more favorable will be the prognosis.
3. The duration of the treatment is therefore to be decided on the basis of the results of the serologic examination.
4. The treatment may last for a few months, or in obstinate cases for years.
5. Neither mercury nor arsphenamin can be employed alone for protracted continuous treatment.
6. A certain risk accompanies the administration of mercury and arsphenamin simultaneously, so that, for a continuous effect to be obtained, periods of mercurial treatment alone should alternate with periods of treatment with arsphenamin alone.
7. However, for abortive treatment in the physically fit, mercury and arsphenamin may at first be administered simultaneously.

At least 2 gm. of arsphenamin should be given during each series (twenty to forty-five days). In the mercury course of about forty days, the soluble salts are used, except for the last two or three injections when gray oil is used to secure a "depot effect." The usual precautions must be taken to avoid a possible Herxheimer reaction. After an apparent cure, the case must be kept under observation for at least two years.

Several cases are related in which this treatment proved successful. However, it is rather troublesome and expensive for the patient, and indeed, says Almkvist, it has not yet had a sufficiently thorough trial to warrant definite conclusions.

Parkhurst, New York.

LA SIFILIDE GASTRICA (GASTRIC SYPHILIS). Alberto Furno, Riv crit. di clin. med. **21**:157, 169 (May 15 and 25) 1920.

Furno states that pain in the epigastrium that is exclusively nocturnal and is associated with anacidity awakens a suspicion of gastric syphilis. Further indications are symptoms of gastric ulcer (hematemesis, melena) in subjects whose gastric chemism is characterized by anachlorhydria or at least hypacidity, low pepsin values and deficient digestive power; also linitis plastica and hour-glass constriction of the stomach. The presence of normal gastric digestion or of hyperchlorhydria excludes the possibility of gastric syphilis. The therapeutic test is, however, the most certain and the easiest means of establishing a diagnosis. Any persistent gastropathy that is rebellious to treatment, and whose symptomatology is unusual either as regards its clinical course or its peculiar signs, should be subjected to syphilitic treatment. The roentgenologic examination may be useful in the diagnosis of gastric syphilis, but it cannot be regarded as decisive. The gastric disturbances may be due to a pyloric stenosis or to a tumor infiltrating the walls, the antrum or the fundus of the stomach, but not presenting the typical aspect that characterizes syphilis. Hour-glass constriction has come to be recognized as frequently due to a modification of the structure of the stomach due to gummatous infiltration and syphilitic cicatrization, but it is necessary to exclude the possibility of its being due to purely functional change, such as atonia, spasm or extragastric compression. The genesis of any anatomic change must be examined carefully, since peptic ulcer or a neoplasm may easily be the inducing cause.

H. R. W., Chicago.

ON THE TREATMENT OF LUPUS VULGARIS BY THE LIQUID ACID NITRATE OF MERCURY. H. G. ADAMSON, Brit. M. J. **2**:123 (July 24) 1920.

Adamson has recently employed the liquid acid nitrate of mercury in a large number of cases of lupus vulgaris, and he believes that he has found in this application a remedy of the selective caustic type which far surpasses any other method of treating lupus in its efficacy and in its rapidity of action.

The patients that have been treated by this method in the skin department at St. Bartholomew's Hospital may be arranged in four classes:

1. Single patches of nonulcerated lupus from the size of a shilling to that of half a crown, and which have received no previous treatment.
2. Old cases of lupus which have been treated by other methods, but in which lupus nodules still remain in the scars.
3. Ulcerated lupus, often of large extent and with much surrounding inflammatory infiltration.
4. The common type of lupus of the nose, involving frequently also the nasal septum, the palate, the upper lip, the cheek and sometimes the lacrimal sac and skin over and around, a type very difficult to deal with by Finsen light or by scraping.

The liquid acid nitrate of mercury is applied by means of a small swab of wool, tightly twisted around the ends of a finely pointed pair of forceps. It is painted on the affected areas freely and with firm pressure, for from one to two minutes, taking care to limit the application exactly to the lupus patches, to isolated nodules, or to ulcerated surfaces. No dressing is applied; a crust generally forms which falls in a few days, and leaves the affected area sometimes completely healed, sometimes as a shallow ulcer which heals in a few days.

In cases of ulcerated lupus, the solution is freely painted on the ulcerating surfaces. This causes considerable pain, but can usually be borne. The surface of the ulcer becomes dry, yellowish white, but in a few days much serous exudation gives rise to a thick, heaped-up crust. At the end of a week the crusts are picked off or bathed off, and there is then an ulceration with purulent surface, which heals in the course of a week or so. The number of applications required in ulcerated lupus depends on the depth of the inflammatory infiltration which often accompanies these ulcerations.

The good results the author has obtained seem to justify a more general use of the acid nitrate of mercury in the treatment of lupus.

Oliver, Chicago.

INFECTIOUS ECZEMATOID DERMATITIS. Richard L. Sutton, J. A. M. A. **75**:976 (Oct. 9) 1920.

In a series of seventy-four cases selected at random and scattered over a period of two years, Sutton found a record of concurrent urticarial eruptions in nineteen instances (more than 25 per cent.). The antecedent disorders varied greatly. As a rule the anaphylactic manifestation did not appear until after the staphylococcic disorder was well under way. All of the attacks were nonfebrile. As a rule, the earlier lesions were frankly suppurative (of fourteen cases in which cultures were made, *Staphylococcus aureus* was recovered in eleven) and auto-inoculable. In the earlier stages of the disease, Sutton has found that a mild astringent, such as an aqueous solution of aluminum acetate (0.5 per cent.), or even lead and opium lotion (lotio opii et plumbi subacetatis) is more effective than one of the greasy preparations. At the end of forty-eight or seventy-two hours, however, one may profitably begin the use of a weak ammoniated mercury ointment (2 per cent.) together with a bland dusting powder containing a small amount of boric acid. After the tendency to suppuration has been overcome, phenolated zinc oil may be substituted for the mercurial ointment. For the relief of the pruritus which often accompanies the urticarial lesions, calamine lotion, to which liquor carbonis detergens (from 2 to 10 per cent.) has been added affords much relief. If necessary, a small amount of phenol (1 per cent.) or menthol (0.5 per cent.) may be added to the ammoniated mercurial preparation, and the ointment used in conjunction with the lotion. Internally, alkaline preparations, such as sodium acetate and sodium citrate in large doses, combined, if the patient is nervous and irritable, with the sodium bromid, frequently prove helpful. If these two fail, Sutton has found the most serviceable remedy to be a mixed staphylococcus vaccine. The initial dose should be small (from 25,000,000 to 75,000,000), and he usually repeats the injections every third day, gradually increasing the amount each time.

Waugh, Chicago.

UEBER TERPENTINOLBEHANDLUNG (KLINGMULLER) MIT BESONDERER BERUEKSICHTIGUNG IHRER ANWENDUNG IN DER DERMATOLOGIE (TURPENTINE OIL WITH ESPECIAL REFERENCE TO ITS USE IN DERMATOLOGY). Heinrich Becher, Dermat. Wchnschr. **71**:460 and 481 (July) 1920.

This is also an extensive review of the literature dealing with the use of intramuscular injection of the oil of turpentine as a therapeutic agent. It has been mostly used in trichophytosis but to some extent in other diseases of the skin. Eighty-one patients were treated. Excellent results were obtained in buboes, soft chancre, eczema, furunculosis, sweat gland abscesses and mastitis. Good results were obtained in prurigo, pruritis, pyodermia in adults, drug rashes, and some gonorrheal affections. It was an aid to the treatment of ulcus cruris, trichophytosis. No benefit was obtained in treatment of impetigo contagiosa, pyodermias of children, chronic prostatitis and gonorrheal arthritis.

The dose established toward the end of the series was 1 c.c. of a 10 per cent. mixture of oleum terebinthinae in olive oil. The interval between injections was not stated, but it was apparently about every four days. The author emphasizes that no untoward results are obtained in this method of treatment, if a strictly pure drug is used. The cases of severe general reactions and albuminuria which have been reported, he is inclined with Karo to attribute to impurities in the turpentine oil. To avoid this he recommends the use of a constant preparation such as "terpichin."

The author emphasizes the importance of giving the drug according to the recommendation of Klingmüller; this is directly on to the muscular fascia about one to two finger breadths below the iliac crest in the posterior axillary line. The article is concluded with a consideration of the various theories concerning the method of action of oil of turpentine as a therapeutic agent.

Ketron, Baltimore.

UEBER LUNGENBEFUNDE BEI MYKOSIS FUNGOIDES UND IHRE BEDEUTUNG (CONCERNING THE LUNG FINDINGS IN MYCOSIS FUNGOIDES AND THEIR SIGNIFICANCE). Erich Kuznitzky, Arch. f. Dermat. u. Syph. **123**:453, 1916.

The study of the lungs in Boeck's sarcoid has led to the conclusion that no association exists between tuberculosis and sarcoid, but that one should consider a specific, primary general disease of the internal organs with localization in the skin, and with great regularity also in the lungs. It appears to belong to the group of chronic infectious inflammatory granulomas, of which the etiologic factor has not yet been demonstrated.

Three cases of mycosis fungoides have been studied to date with the object of adding mycosis fungoides to the group of infectious granulomas. Unfortunately, the cases represented the three periods of the disease.

Lung changes were not demonstrable clinically, but the roentgen ray demonstrated changes similar to those of Boeck's sarcoid. In two cases the lung changes were marked. There was a shadow over the lung area, the apexes were clear, and there was an accentuation of the bronchial tube shadows. About the hilus, there was some enlargement and increase of the normal shadow. There was no evidence of inflammatory changes. It is difficult to give an analysis of the findings. The von Pirquet test was negative in all three cases. Subcutaneous tuberculin injections in two of the cases resulted in no diagnostic rise in temperature in one case. Apparently, a case of mycosis fungoides can be considered as showing the lung changes mentioned. In addition, the perivascular lymphoid infiltration, the leukopenia, liver and spleen enlargement, and hyperplasia of the lymph glands link Boeck's sarcoid and mycosis fungoides in the group of infectious inflammatory chronic granulomas.

Goodman, New York.

UEBER DAS WESEN DER "DYSIDROSIS" (THE SUBJECT OF DYSHIDROSIS). M. Ota, Japan. Ztschr. f. Dermat. u. Urol. **20**:6 (June) 1920.

Two years ago the writer published a paper on the same subject, in which he stated that vesicular and squamous diseases of the hands and feet due to trichophyton infection resemble the lesions described under the heading of pompholyx. This observation had been previously reported by Marie Kaufmann-Wolff and by Max Schramek. The writer at that time considered all these affections of the hands and feet, with few exceptions, as ringworm affections.

Kamibayashi agreed with the author in certain points, but also believed that a distinct entity existed to which he gave the name of idiopathic pompholyx to avoid confusion with a type of pompholyx due to fungi infection.

There are cases of vesicular dermatoses from which the fungi cannot be isolated. There are also cases in which fungi have been found in the feet but not in the affected hands. Is it probable, then, that in such cases the feet are infected by fungi while the hands are the sites of dyshidrosis? There are also cases in which the clinical signs are those of dyshidrosis without positive findings of fungi and yet the lesions disappear under antiparasitic treatment. Do not these facts lead us to the supposition that the majority of such cases bear a certain relationship to fungi infection?

Levin, New York.

ELECTRICAL DANGERS IN X-RAY LABORATORIES. J. S. Shearer. Am. J. Roentgenol. **7**:432, 1920.

The recent death of Dr. Jaugeas by electrocution in a roentgen-ray laboratory in Paris serves to direct attention to the danger of operating roentgen-ray devices when proper precautions are neglected, or when the idea of safety is based on a misconception of the fundamental facts involved. The article by Dr. Shearer must be read in toto to be appreciated, for it does not lend itself very readily to abstracting. The closing paragraph is worthy of repetition here:

". . . medical colleges may some day come to realize that special training is needed for those who are to utilize such powerful agencies in their profession. It is quite true that there is not time to train all medical practitioners in all topics, but there should be provided opportunity for those who do specialize in radiology to secure adequate training When this is accomplished this practice should be restricted to medical graduates who have, in *addition* to the regular medical course, such special training as is needed to increase both the usefulness of this agent and the safety of all concerned."

Goodman, New York.

RUBBER TUBING AS A FACTOR IN REACTION TO THE BLOOD TRANSFUSION. George J. Busman, J. Lab. & Clin. M. **5**:693 (Aug.) 1920.

The author reports the results of his experiments on blood transfusion with rubber tubing of a certain brand with the following conclusions:

1. The brand of supposedly pure gum rubber tubing, which in preliminary experiments by Stokes and Busman produced a reaction in arsphenamin administration, is apparently also able, when new, to produce a reaction if used in blood transfusion work.

2. The toxic substance is taken up in sufficient amounts to produce a reaction in patients receiving transfusions of citrated blood through 80 cm. of new rubber tubing of 4 mm. internal diameter.

3. Enough of the toxic agent is taken up by 250 c.c. of normal uncitrated blood drawn through as little as 35 cm. of new rubber tubing (internal

diameter, 4 mm.), en route from the vein to the container of citrate solution, to produce distinct reaction when given through an old tube. It is not, therefore, necessary that whole blood be citrated to absorb the toxic principle.

4. The mechanically removable débris from the inside of new sterilized tubing does not produce reactions when given in suspension in distilled water or 0.18 per cent. sodium hydroxid solution.

5. Further experiment confirms the observations previously recorded that the toxic agent can be removed from the new tubing by soaking it in normal sodium hydroxid solution for six hours.

6. It should be specifically stated that no attempt is made to propose rubber tubing as an explanation of all transfusion reactions which present chills, fever, prostration, etc. Tubing is merely proposed as one factor.

Waugh, Chicago.

EXPERIMENTAL SYPHILIS IN THE RABBIT. IV. CUTANEOUS SYPHILIS. PART 1—AFFECTIONS OF THE SKIN AND APPENDAGES. Wade H. Brown and Louise Pearce, J. Exper. M. **32**:445 (Oct.) 1920.

Skin lesions were found to be most abundant and varied in generalized syphilis in rabbits, the manifestations being chiefly alopecias, paronychia, onychia and lesions of the skin proper.

Several varieties of alopecia were noted, the first of which produced an appearance similar to moth-eaten alopecia in the human being; the second was an abnormal looseness of the hair in large areas; the third was associated with definite skin lesions. Paronychia and onychia were infrequent.

The skin lesions consisted of granulomas which resembled the primary scrotal lesions: cutaneous infiltrations of two types, a flattened and diffuse process and an elevated circumscribed papule.

Macular erythemas were also noted which resembled the human type, although they were not definitely shown to be of specific orgin.

EXPERIMENTAL SYPHILIS IN THE RABBIT. IV. CUTANEOUS SYPHILIS. PART 2—CLINICAL ASPECTS OF CUTANEOUS SYPHILIS. Wade H. Brown and Louise Pearce, J. Exper. M. **32**: 473 (Oct.) 1920.

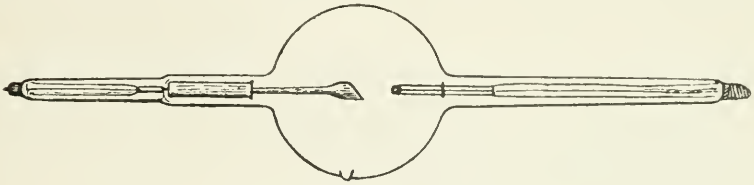
The lesions of the skin manifested in the rabbits studied showed a predilection for certain areas, the character of the lesions differing somewhat in the various locations. The head lesions were mostly small papules or diffuse infiltration; on the forearms and feet they were also of a large granulomatous type, the latter type predominating on the hind feet and legs. It was noted that when multiple lesions appeared in any one area, most of the lesions ceased growing, allowing one or two to reach a considerable size.

The first cutaneous eruption was found to occur approximately from two to four months after inoculation, the earliest being three weeks, the latest two years and eight months. Successive crops of lesions may appear, the duration of lesions varying from a few days in the erythemas to two years in the granulomas. All observations tended to show that the infection had an essentially relapsing course.

Jamieson, Detroit.

RADIOTHERAPIE PROFUNDA (DEEP ROENTGEN-RAY THERAPY). JOSE GARCIA DONATO and VICENTE GARCIA DONATO, Los Prog. de la Clin. **8**:392, 1920.

A reaction following deep roentgen-ray has been described, the symptoms of which are not unlike those following arsphenamin injections, namely, headache, nausea, diarrhea and other symptoms. Several names have been given, e. g., "Roentgenkater," "Roentgenaterpia," and simple "Roentgen toxemia." The treatment is cessation of the exposures.



A Fuerstenau modification of the Coolidge tube.

GOODMAN, New York.

THE TREATMENT OF SYPHILIS. WALTER J. HIGHMAN, Med. Rec. **98**:477 (Sept.) 1920.

Highman has found the several brands of arsphenamin on the market to be of about equal therapeutic value. He says that any brand which has passed the test of the Hygienic Laboratory in Washington is safe.

The arsenic of an arsphenamin molecule is attached to the spirochete by the benzol ring and brings about a disintegration of the micro-organism. Twenty c.c. of water are used to each decigram of the drug and sodium hydrate is used in excess of the amount needed for clearing the precipitate as a slight overalkalinization is thought to be less toxic.

The author describes in detail the method of injection and suggests the use of a permanent suspension, as supplied by Lowry, for those whose limited experience does not warrant the use of the more difficult method. Mercury salicylate, in conjunction with arsphenamin is used in weekly injections. Intervals of treatment lasting from eight to fifteen weeks are followed by an interval of rest.

The stage of the disease and the results of treatment, as shown by the Wassermann reaction, are used as guides for the amount of treatment needed.

TOMLINSON, Omaha.

LA BOUBA BRASILIANA E UNA LEISHMANIOSI GUARIBILI MEDIANTE IL TARTARO STIBIATO (BRAZILIAN BOUBA IS A LEISHMANIOSIS CURABLE BY TARTAR EMETIC). A. BREDA, Gior. ital. d. mal. ven. **61**:306 (Aug. 12) 1920.

The author, who has been studying the subject since 1895 and has written extensively concerning it, reminds us that kala-azar (produced by Leishmania donovani) and oriental sore (produced by Leishmania tropica) are diseases due to parasites of the same family. He has found similar protozoa in cases of Brazilian boubas and in the diseases known as Baurú ulcer and pian-bois, which Breda asserts ought to be classified together in the same group of diseases due to the leishmanias. In 1913, Vianna of Brazil used for the first time tartar emetic in the treatment of these diseases. His gratifying results led others to try the new drug, and since then it has been proved without doubt that it is a specific for these diseases. The author reports two cases of extensive and destructive lesions of boubas affecting the extremities, the nose and the mouth, which were entirely cured by intravenous injections of tartar emetic (0.05 gm. in 5 c.c. of sterile water).

PARDO-CASTELLO, Havana.

UEBER EINEN DER PARAKERATOSIS VARIEGATA (UNNA) BZW. PITYRIASIS LICHENOIDES CHRONICA (NEISSER-JULIUSBERG) NAHESTEHENDEN EIGENTUEMLICHEN FALL (A PECULIAR CASE CLASSIFIED AS PARAKERATOSIS VARIEGATA OR PITYRIASIS LICHENOIDES CHRONICA). VIKTOR MUCHA, Arch. f. Dermat. u. Syph. **123**:586, 1916.

A healthy young man, with no hereditary taints, had noticed for fourteen days a generalized eruption of the entire body which gave no subjective symptoms. The erythema was polymorphous, showed macules, slight scaling, papular and papular-necrotic efflorescences, but slightly inflamed, yet decidedly infiltrated, which healed spontaneously, in part without changes in the skin, and in part with scar formation somewhat like that of variola.

The histologic findings in the fresh lesions showed a high grade edema of the upper strata of the cutis and epidermis with a marked epithelial change, massive, extensive perivascular infiltration, especially in the upper layer of the cutis. In the older lesions, the edema was less, but the perivascular infiltration encroached on and ruptured the epidermis. In the central parts were regressive changes in the form of increased cornification and beginning crust formation.

In the differential diagnosis these conditions were considered in the order given: maculopapular or papulonecrotic syphilid; an atypical variola; a tuberculid, and parakeratosis variegata or pityriasis lichenoides chronica, although no mention has ever been made of the presence of necrosis in this affection, and despite the very short course of the disease.

GOODMAN, New York.

VENIPUNCTURE IN THE TREATMENT OF CERTAIN DISEASES OF THE SKIN. JEROME KINGSBURY and PAUL E. BECHET, J. A. M. A. **75**:937 (Oct. 2) 1920.

Kingsbury and Bechet believe that venipuncture is of occasional value in certain asthenic cases of psoriasis, erythema multiforme and dermatitis herpetiformis. It is of great value in the treatment of urticaria, and in their hands affords more relief in severe cases of that disease than any other therapeutic method. They recommend a platinum needle of fairly large caliber (from 16 to 14 gage). The amount of blood withdrawn varies from 100 to 250 c.c., depending on the general condition of the patient. The authors usually bleed the patients once or twice a week. The method is more or less empiric. It has a detoxicating and depurative action on the blood, stimulating the excretory organs, increasing antitoxins, and regenerating the blood mass. In psoriasis, bloodletting seems to be of value in the acute cases with intense congestion around the lesions. The patients were invariably benefited. In erythema multiforme, it is a therapeutic adjuvant of very distinct value. In dermatitis herpetiformis, venipuncture repeated systematically invariably improves the condition of the eruption and relieves the subjective symptoms. The most gratifying results, however, were obtained in urticaria, particularly in that type of the disease with large raised wheals and associated angioneurotic edema with intense pruritus.

Waugh, Chicago.

SKIN INVOLVEMENT IN BREAST CANCER, WITH REFERENCE TO ITS BEARING ON THE INTERPRETATION OF APPEARANCES OF TRANSITION BETWEEN NORMAL EPITHELIUM AND CANCER. Alson R. Kilgore, J. Cancer Res. **5**:291 (July) 1920.

This investigator takes issue with Janeway and Ewing, who express the belief that there is a transformation of normal epithelium into neoplastic tissue, and supports Borrmann, Ribbert and Rous in their contentions that such a transformation is only apparent and that the existing condition is merely a secondary union of the two types of cells due to close approximation. In 475 specimens of breast cancer, seventy-four showed histologic involvement of the skin, but only sixteen showed intimate approximation of cancer to epithelium. Of these, seven showed apparent histologic union but no suggestion of transformation of nonmalignant into malignant cells. In all of these seven cases there was hyperplasia of the normal epithelium, and it was pointed out that the variations in normal cell types associated with hyperplasia lent themselves to the suggestion of transition forms from epithelium to cancer. The morphologic differences between breast cancer cells and skin epithelial cells serve to identify the two types at the point of secondary union.

H. R. Foerster, Milwaukee.

SUR LA SYPHILIS CONGENITAL DE LA SECONDE GENERATION (CONGENITAL SYPHILIS OF THE SECOND GENERATION). E. Bruusgaard, Acta Dermato-Venereologica **1**:1. 1920.

With the increasing efficiency of antisyphilitic treatment, the disease will more rarely be transmitted to the second generation. In his hospital service the author recently saw a boy of 8 years who presented rhagades about the mouth and serpiginous scarring on the abdomen. The Wassermann reaction was strongly positive. At the age of 1 month, according to the history, there had been an eruption about the mouth, on the extremities and on the abdomen, for which mercurial baths had been given.

The mother, aged 25 years, had had no other children, or any miscarriages. She presented an old bilateral tibial periostitis and the remains of a parenchymatous keratitis which had been active at the time of her confinement. At that time, too, she had suffered from ulcerations of the right leg, and received mercurial inunctions. Her blood gave a strongly positive Wassermann reaction. Furthermore, her history revealed that she had had an eruption involving the face and body when 6 months old, for which she had received mercurial baths. The possibilities of reinfection or superinfection were carefully ruled out.

The maternal grandmother had been infected by her husband; from this infection had resulted a tertiary tibial periostitis accompanied by gummas. Pregnant nine times, she had suffered two miscarriages; three of her children had died in infancy with the signs of congenital syphilis, and another had died at the age of 8 years with a congenital defect. Of the three survivors, one presented definite syphilitic stigmas and a positive Wassermann reaction, while the second showed neither. The eldest was the mother of Bruusgaard's patient.

Parkhurst, New York.

LA NOUVELLE LOI SUEDOISE SUR LES MALADIES VENERIENNES (THE NEW SWEDISH LAW REGARDING VENEREAL DISEASES). Karl Marcus, Acta Dermato-Venereologica **1**:62, 1920.

The fundamental principles of the enactment are:

1. An extended service for information and instruction.
2. The obligation of every one contracting a venereal disease to seek the advice of a physician and to conform to his orders.
3. The right of every patient to receive free treatment.
4. The application of certain coercive measures.

The author gives a complete analysis of the various articles. The contagious period is defined, and its vagueness is recognized. If need be, the patient may be placed in a hospital, and here the author advises general adoption of the scheme in vogue at the hospital of St. Göran. Patients with venereal diseases are not placed in a separate ward, but in the general wards side by side with other patients. Thus the stigma usually attached to venereal diseases is largely avoided and, according to the author, the risk of contagion to neighboring patients is nil.

A fund is provided by public taxation to defray the expenses of treatment, both in hospitals and in dispensaries. The patient may choose his own physician, but he is compelled to seek medical advice immediately. Having diagnosed the disease, the physician must notify the patient regarding it and also give information concerning the treatment, prevention of transfer and postponement of marriage until a cure is effected or the contagious period is over. An attempt is also made to ascertain the source of infection in each case. The rules of professional secrecy hold good here as elsewhere, and safeguard the law-abiding patient against any possibility of stigma.

In concluding, Marcus reminds the practitioners that the degree of success of this law will be in direct proportion to the degree of energy and enthusiasm with which they cooperate in its behalf.

Parkhurst, New York.

STATUS OF THE LUETIN TEST. Louis Hannan, Med. Rec. **98**:522 (Sept.) 1920.

Of 100 unselected cases, eleven patients reacted positively to the luetin test. None responded to antisyphilitic treatment.

In checking the influence of medication on the test, mercury and iodids were given for two to three days prior to the application of the luetin, and in thirty consecutive cases the reaction was positive.

Mercury alone was given to ten apparently normal persons, and the luetin tests made following its use were all negative. Some time later six of the ten were tested in a similar way substituting iodid for mercury, and all reacted positively.

The author concludes that the drug reactions are due solely to the iodid, and that the test as now used is unreliable and should be eliminated from standard textbooks.

Tomlinson, Omaha.

MENINGO-MYELITE SYPHILITIQUE DE LA REGION DORSO-LOMBO-SACREE (SYPHILITIC MENINGOMYELITIS OF THE DORSOLUMBOSACRAL REGION). J. H. Laliberte, Bull. méd. de Quebec **20**:321 (July) 1920.

Laliberte's patient, a man, aged 34, who presented a paraplegia of the legs, suffered in addition other motor and sensory disturbances, changes in the tendon reflexes, and disturbances of anal and vesical sphincter reflexes. The history and clinical findings indicated a lesion involving all the cord tissue beneath the tenth and eleventh dorsal vertebrae, involving certain parts more than others, and the meninges as well. The pathologic process consisted of a sclerosis affecting the nerve elements controlling sensation, motion and nutrition of the affected parts.

Tuberculosis, syringomyelia and multiple sclerosis had to be considered in the diagnosis as well as tabes dorsalis; but all of them could be excluded, leaving a diagnosis of syphilitic meningomyelitis of the dorsolumbosacral region. Under antisyphilitic therapy, the patient's condition improved remarkably, and he refused to remain under observation longer.

Senear, Chicago

ERYTHEMA BULLOSUM VEGETANS. B. Lipschutz, Arch. f. Dermat. u. Syph. **123**:523, 1916.

A girl, aged 22, presented on the backs of both hands serous and seropurulent bullae that fitted the well-known picture of erythema bullosum. A unique feature of the case was that previous to the rupture of the bullae, there were formed on their sites smooth elevated, or semispherical buttonlike vegetations. There could be no question of secondary infection, and there was no evidence of systemic disease. In a few weeks, the patient was entirely well. Microscopic and bacteriologic examinations were all negative. The differential diagnosis required finding an affection of papular vegetating efflorescence following bulla formation. Among those known, pemphigus vegetans, dermatitis pseudo-syphilitica vacciniformis, and a disease presenting similar characteristics reported by Reine (later diagnosed mycosis fungoides) were easily distinguished.

The histopathologic findings deserve further study, but from the consideration of description, the condition deserves the application of erythema bullosum vegetans.

Goodman, New York.

NUOVO CONTRIBUTO ALLO STUDIO DELLE LESIONI DEL NERVO ACUSTICO NELLA SIFILIDE RECENTE (FURTHER CONTRIBUTION TO THE STUDY OF THE LESIONS OF THE ACOUSTIC NERVE IN EARLY SYPHILIS). J. Capelli and C. Torrigiani, Gior. ital. d. mal. ven. **61**:243 (Aug. 12) 1920.

The authors report seven cases of acoustic disturbances occurring early in the secondary period of syphilis. All the patients were more or less rapidly affected with sudden deafness of one or both sides, accompanied by dizziness with crisis of vertigo. From the authors' statistics, they conclude that the eighth is the cranial nerve most commonly affected in the secondary stage of syphilis. Acoustic neuritis is frequently accompanied by neuritis of the facial and of the oculomotor nerves. The majority of the patients improve rapidly under specific therapy, but return to normal very seldom occurs.

Pardo-Castello, Havana.

A SERUM AGAINST SOFT CHANCRE, ESPECIALLY ITS BUBOES.

John Reenstierna, Acta Dermato-Venereologica **1**:146, 1920.

Dead and living streptobacilli were intravenously injected into rams, and the resultant serum was found to agglutinate Ducrey bacilli. This serum has been proved effective therapeutically, and its activity is further enhanced by the addition of a certain quality of dead "feverizing" bacteria (e. g. the typhus bacillus). Previously obstinate lesions have healed rapidly under this treatment, aided, of course, by the usual local therapy. The period of treatment of the buboes, which previously according to many statisticians had been a month or more, has been brought down to somewhat more than one week.

The inconveniences of this treatment are chills and fever after the injection, considerable tenderness for several days at the seat of injection, and sometimes a passing tenderness in regionary lymph nodes.

Parkhurst, New York.

UEBER EINE EIGENARTIGE VERFAERBUNG DER HAUT UEBER DEN VENEN DER VORDERARME NACH ANWENDUNG VON CHYSAROBIN (A PECULIAR DISCOLORATION OVER THE VEINS OF THE FOREARM AFTER THE USE OF CHRYSAROBIN).

H. Fischer, Dermat. Wchnschr. **71**:582 (Aug.) 1920.

In the case reported the patient had been using a 1 per cent. chrysarobin paste and had taken Fowler's solution internally. He had the usual pigmentation about the psoriasis lesions over the body, but over the veins of the forearm the discoloration was much intensified forming dark lines running up and down the arms. This must have been caused by a greater oxidation of the chrysarobin over the veins, but no definite reason for this could be ascertained, although some theoretical possibilities were considered.

Ketron, Baltimore.

UEBER EINE BEZIEHUNG DER GRIPPE ZUR LUES (RELATION OF INFLUENZA AND SYPHILIS).

Pauls Neuda, Wien. klin. Wchnschr. **33**:796, 1920.

Analysis of the case histories of influenza among syphilitic patients gives the impression that the disease runs a lighter course than among non-syphilitic patients. The syphilitic infection is also apparently altered, as shown by the change of the Wassermann reaction toward negative, and an improvement in the findings of the cerebrospinal fluid. The colloidal reaction remains unchanged, however, so that one may not believe that the syphilitic infection is ameliorated, but that the influenza appears to have the power of binding the power of the Wassermann reaction. As other diseases, croupous pneumonia and erysipelas, for example, also have the tendency to alter the Wassermann reaction in syphilitic patients, it would be interesting to observe whether these run a milder course in syphilitic than in nonsyphilitic patients.

Goodman, New York.

A CASE OF LEUKEMIA WITH SCALP NODULES.

T. H. Gunewardene, Brit. J. Child. Dis. Nos. 193-195:9 (Jan.-March) 1920.

A boy, aged 3½ years, developed more than a dozen pale half inch nodules on the scalp about three months after an attack of measles. The appearance of the nodules was associated with a change in the blood picture from that of a secondary anemia to that of myeloid leukemia. The nodules increased in number and size and spread to forehead and eyebrows with a decline of the patient's condition, many of them disappearing or decreasing in size just before death. The nodules microscopically showed closely packed aggregations of large mononuclear cells in the muscle layer.

H. R. Foerster, Milwaukee.

EIN BEITRAG ZUR AETIOLOGIE VON VITILIGO VULGARIS MIT BESONDERER BERUECKSICHTIGUNG SEINER BEZIEHUNG ZUR SYPHILIS UND DEN NAEVI (A CONTRIBUTION TO THE ETIOLOGY OF VITILIGO VULGARIS WITH SPECIAL REFERENCE TO SYPHILIS AND NEVI). Shin'ichi Sasamoto, Japan. Ztschr. f. Dermat. u. Urol. **20**:5 (May) 1920.

During the past year the writer studied forty-two cases of vitiligo with special care to determine the relationship of this condition to syphilis. Of the twenty-two patients, who were 20 years of age or older, twelve showed positive signs of syphilis and positive Wassermann tests. In one case there was tabes with the characteristic pupils, reflex signs and lancinating pains. In one case the skin changes disappeared after treatment with arsphenamin and mercury.

In the remaining patients, younger than 20 years, three showed positive signs of erbsyphilis, and in five the Wassermann reaction proved positive. Two of these cases showed positive signs of hereditary syphilis.

Levin, New York.

LA DIFFUSIONE DELLA LEBRA IN SARDEGNA ED IL PRIMO SPERIMENTO DI LOTTA ANTILEBBROSA ESEGUITO IN ITALIA (THE SPREAD OF LEPROSY IN SARDINIA AND THE FIRST ATTEMPT OF AN ANTILEPROSY CAMPAIGN IN ITALY). F. Radaeli, Gior. ital. d. mal. ven. **61:** (Aug. 12) 1920.

The author was a member of a special committee appointed by the Italian government in 1911 to study the problem of leprosy in Italy. In Sardinia, leprosy is widespread. In a small town of 4,000 inhabitants, he found seventeen lepers. Oil of chaulmoogra was used by mouth, as much as 400 drops being given daily. Good results were also obtained with certain proprietaries. Locally, the roentgen ray, ultraviolet rays, carbon dioxid snow and radium were used with advantage in the ulcerative and destructive lesions.

Pardo-Castello, Havana.

UEBER CHLAMYDOZOA-STRONGYLOPLASMEN. IV. UEBER DAS VORKOMMEN VON ZELLEINSCHLUESSEN BEIM IDIOPATHISCHEN HERPES ZOSTER (CHLAMYDOZOA-STRONGYLOPLASMA. IV. CONCERNING THE OCCURRENCE OF CELL INCLUSIONS IN IDIOPATHIC HERPES ZOSTER). B. Lipschutz, Wien. klin. Wchnschr. **33**:836, 1920.

Lipschutz continues his studies and makes his fourth literary contribution concerning the etiology of herpes zoster. He has had the opportunity of studying the skin in cases of zona by modern methods of intravital staining, etc. He is convinced that the "zoster-corpuscles" have some relation to the disease, and that the reaction formerly described in the nuclei of the cells of the rete is a specific one. Experimental work, already completed and apparently successful, will be reported in a later communication.

GOODMAN, New York.

VENEREAL PROPHYLAXIS IN CIVILIAN LIFE. H. L. SANFORD, J. Urol. **4**:383 (Aug.) 1920.

This article is a plea for the establishment of prophylactic stations for the prevention of disease rather than the indiscriminate use of prophylactic packages by exposed persons. The author believes the station method is much more efficient, although the alternative is better than none.

Estimate is also made of the financial loss in Ohio in one year from venereal diseases. This is stated to be as high as $50,000,000, due to first treatment, loss of time from work, later treatment, complete or partial disability, shortening of life, etc.

He believes in the support of the moral and social agencies now working, and hopes prophylaxis can be added later.

JAMIESON, Detroit.

UEBER NEKROTISIERENDE HAUTHAEMORRHAGIEN BEI HAEMORRHAGISCHEN VARIZELLEN (NECROTIZING SKIN HEMORRHAGES IN HEMORRHAGIC VARICELLA). GUSTAV MORAWETZ, Arch. f. Dermat. u. Syph. **123**:579, 1916.

During the course of hemorrhagic varicella, a boy, aged 3, developed very unusual features as a complication. The ordinary varicella lesions became hemorrhagic, showed evidence of pus formation and led to necrosis, not only at the site of the original varicella lesion, but more extensive, so that large areas were gangrenous. The lesions began to granulate in about four weeks, an accompanying nephritis and bronchitis began to clear up, and the patient was discharged after eight weeks. A colored illustration of the clinical condition accompanies the article.

A MODIFICATION OF HARRISON'S TREATMENT FOR RINGWORM OF THE NAILS. ANDREW L. GLAZE, J. A. M. A. **75**:743 (Sept. 11) 1920.

Harrison advises scraping the nail and then applying on lint, for fifteen minutes, one part of potassium iodid in eight parts of a 50 per cent. solution of potassium hydroxid. Afterward, mercuric chlorid, 1 per cent. in equal amounts of alcohol and water, is kept in contact for twenty-four hours. In most cases it is difficult to scrape away the roughened nail, and the application of the potassium preparation on lint has certain disadvantages. By the method described below, the remedy is confined to the plate and matrix, and the horny tissue is easily removed.

If the fingernails are to be treated, the patient grasps a towel-covered book so that the parts are supported in a horizontal plane. Petrolatum is generously banked about the nails in such fashion that each forms the bottom of a little lake. These are half filled with Harrison's potassium solution, and the softened plate is scraped through the fluid.

The after-treatment with mercuric chlorid sometimes causes severe dermatitis. In its place Glaze has used with safety, and relative satisfaction, a saturated solution in water of sodium thiosulphate (hyposulphite). It is applied on absorbent cotton, under a rubber fingerstall, six hours or longer, daily for three days.

WAUGH, Chicago.

HEMANGIOMA AND LYMPHANGIOMA; THEIR RESPONSE TO THE INJECTION OF BOILING WATER. FRANCIS REDER, Med. Rec. **98**:519 (Sept.) 1920.

Reder treated 200 cases of hemangioma by injections with boiling water, with uniformly good results. Only five patients became infected and they responded promptly to aseptic treatment. Of eight patients with lymphangioma, two became infected, and although seriously sick, both recovered.

While this method of treatment in lymphangioma is not as encouraging as in angioma, it is considered a valuable asset when intervention seems imperative and operative measures are contraindicated.

TOMLINSON, Omaha.

UEBER DAS STIRNEKZEM INFOLGE HUTLEDERERSATZ UND SEINE URSACHE (ECZEMA OF THE FOREHEAD FROM HAT BANDS, AND ITS CAUSE). GALEWSKY, Dermat. Wchnschr. **70**:353 (June) 1920.

Galewsky reports the frequency in Germany of cases of dermatitis of the forehead due to some irritating substance in hat bands. Due to the scarcity of leather, these bands are made of leather imitations, and the author was able to demonstrate the presence of cresol in them, to which he attributes their irritating quality.

KETRON, Baltimore.

ZUR KENNTNIS DES LICHEN NITIDUS (CONTRIBUTION TO LICHEN NITIDUS). F. LEWANDOWSKY, Arch. f. Dermat. u. Syph. **123**: 494, 1920.

There may still be some relation between lichen nitidus and tuberculosis which has not been suspected. However, to include the affection among the tuberculids is premature. Animal inoculation and the demonstration of the bacillus of Koch (other than in the instance of Arndt) are still lacking. Several clinical characteristics also do not fit the picture of tuberculosis of the skin. Chief among these is the long period in which the affection remains on the same level, without progressing or regressing, which is not noted in any other tuberculid. Localization on the shaft of the penis, a site of predilection of lichen nitidus, is almost unknown for hematogenous tuberculosis. The problem of the specific character of lichen nitidus is not yet answered, but it seems certain that it does not pertain to the group of tuberculids.

GOODMAN, New York.

LINEAR PIGMENTATIONS IN AN ICHTHYOTIC NEGRO. S. MENDES DA COSTA, Acta Dermato-Venereologica **1**:61, 1920.

Apropos of Weidman's article in *The Journal of Cutaneous Diseases*, August, 1919, Da Costa briefly describes a case in which the lines were chiefly transverse and occupied the folds of the skin. The theory is advanced that the pigmentation is due to the penetration of the light into the furrows where the scales are separated. The horny cells were exempt of nuclei, but contained grains and irregular clusters of black pigment, which failed to give an iron reaction.

Parkhurst, New York.

INTRACISTERN INJECTIONS OF SALVARSANIZED SERUM IN NEUROSYPHILIS. Henry McCusker, Boston M. & S. J. **183**:490 (Oct. 21) 1920.

The author cites a case of neurosyphilis in which puncture of the cisterna magna was performed between the occiput and the atlas, and he gives the technic for this procedure.

He further suggests that: "(1) Cistern puncture offers another route of application in the method of therapy in syphilis of the central nervous system. (2) It gets the serum nearer to the seat of the disease. (3) It is easier to accomplish than a spinal tap. (4) It offers no more danger than rhachicentesis."

Lane, Boston.

PROTEIN SENSITIZATION IN ECZEMA OF ADULTS. Howard Fox and Edgar Fisher, J. A. M. A. **75**:907 (Oct. 2) 1920.

An interesting report is made of the experimental work done by the authors using Walker's technic. It seems difficult to draw definite conclusions at present regarding the true value of the protein skin tests in eczema of adults. Most of the published reports have dealt with eczema of infants or children. The authors tested each patient by the cutaneous method with a goodly number of the ordinary commercial proteins. The results of these different methods have varied greatly, and they believe that a good deal of investigation remains to be done to determine the real value of the tests. It would appear, however, that they will ultimately prove to be of therapeutic assistance in a small proportion of cases of eczema of adults.

Waugh, Chicago.

VERAENDERUNGEN DER HAARE UND PILZBEFUNDE IN ZWEI FAELLEN VON CHROMIDROSIS (HAIR CHANGES AND MYCOTIC FINDINGS IN TWO CASES OF CHROMIDROSIS). E. Meirowsky, Arch. f. Dermat. u. Syph. **123**:573, 1916.

Two cases of blue chromidrosis were so similar that one description fitted both. The shaft and bulb showed changes indicating mycotic infection. Analysis revealed what seemed to be mycelia, and stained small round bodies, possibly spores. Whether trichomycosis palmellina has an etiologic relation to chromidrosis has not been proved. That a causal relation exists has been often asserted, and the two have been associated in the experience of several dermatologists.

Goodman, New York.

MUZINOESE BINDEGEWEBSDEGENERATION IN DER HAUT (FAERBUNG IM PARAFFINSCHNITT) (STAINING OF MUCINOUS DEGENERATION OF THE SKIN IN PARAFFIN SECTIONS). C. Kreibich, Dermat. Wchnschr. **71**:539 (Aug.) 1920.

The author asserts that beautiful specimens of mucinous degeneration of the skin are obtained by the method which he describes, and also that there is a saving of the reagents used. This method differs from the usual ones in that the paraffin sections are transferred directly, before removal of the paraffin, into a weak solution of the stain (1 or 2 cm. of stain to 200 or 300 c.c. of warm distilled water). The staining is controlled under the microscope. Afterward the section is transferred to the slide and treated with alcohol, zylol and mounted in balsam.

KETRON, Baltimore.

INVESTIGATIONS RE THE SO-CALLED "MATCH ECZEMA" AND ITS CAUSES. J. STRANDBERG, Acta Dermato-Venereologica **1**:116, 1920.

Considering the number of cases of "match eczema" recently noted, the author undertook a thorough investigation, arriving finally at this conclusion:

The so-called "match eczema" is a toxicodermia caused by sesquisulphid of phosphorus which of recent years has entered as the chief component in the striking-surface of certain matchboxes. Probably, bad glue contributes in causing this skin condition. The use of the sesquisulphid has now been discontinued in the match factories of Sweden.

PARKHURST, New York.

SIFILIDE TERZIARIA DELL'ARTICOLAZIONE DELL'ANCA (TERTIARY SYPHILIS OF THE HIP JOINT). L. MORINI, Gior. ital. d. mal. ven. **61**:251 (Aug. 12) 1920.

Morini presents the case of a man, aged 52, who suffered a fracture of the femur two years after a syphilitic infection. A gumma developed at the site of the fracture accompanied by arthritis. Mixed treatment effected a cure although the movements were never normal on account of a hypertrophic callus. This case is interesting because of its rarity, only two other cases having been previously described by Fournier.

PARDO-CASTELLO, Havana.

ZUR FRAGE: GRIPPE UND LUES (CONCERNING INFLUENZA AND SYPHILIS). MAXIMILLAN STRASSBERG, Wien. klin. Wchnschr. **33**:797, 1920.

The Wassermann reaction in the blood and the laboratory findings in the spinal fluid, other than the colloidal gold reaction, are favorably influenced by the fever of influenza. In a series of secondary syphilitic cases, blood Wassermann reactions were reduced to negative, although the influenza had interrupted the therapeutic attack after the first dose of arsphenamin. Other specific fevers are known to have a similar influence. In these facts are found confirmation for the practice of inducing fever in syphilitic patients by the injection of milk and other proteins, which has been done at the Strassbergs clinic.

GOODMAN, New York.

CONTRIBUTO ALLO STUDIO DELLA STRONGYLOPLASMA HOMINIS DI LIPSCHUTZ (CONTRIBUTION TO THE STUDY OF STRONGYLOPLASMA HOMINIS OF LIPSCHUETZ). A. FONTANA, Gior. ital. d. mal. ven. **61**:409 (Aug. 12) 1920.

Fontana refers to Lipschütz' discovery of a parasite in the lesions of molluscum contagiosum. This parasite is a small corpuscle of circular outline, measuring about 0.16 mikrons. It is always present in the lesions of molluscum in isolated form. It stains well by Loeffler's method or by Fontana-Tribondeau's method with silver. This article is illustrated by seven photomicrographs of the strongyloplasma.

PARDO-CASTELLO, Havana.

FREQUENCY OF SYPHILIS WITH CANCER OF THE LIPS, TONGUE AND BUCCAL MUCOUS MEMBRANE. N. Austin Cary, J. A. M. A. **75**:859 (Sept. 25) 1920.

The author's conclusions are based on a study of 907 case histories from the Surgical Pathology Laboratory of the Johns Hopkins Hospital. Syphilis in association with cancer of the tongue is approximately three times more common than in other locations about the mouth—14.5 per cent., or about one in seven cases. This very fact is urgent reason against protracted antisyphilitic treatment in tongue lesions which may be cancer, even in the presence of positive evidence of syphilis. Regardless of the causal relationship of syphilis to cancer, once a neoplasm has been established the prognosis is that of cancer and not of syphilis, and treating the syphilis will not affect the cancer, but will only delay urgently needed surgery.

Waugh, Chicago.

ZUR DIFFERENTIALDIAGNOSE ZWISCHEN MIKROSPORIE UND OBERFLAECHLICHER TRICHOPYTIE DES BEHAARTEN KOPFES (THE DIFFERENTIAL DIAGNOSIS BETWEEN ALOPECIA DUE TO MICROSPORON AND SURFACE TRICHOPHYTOSIS OF THE HAIRY SCALP). Robert Otto Stein, Wien. klin. Wchnschr. **33**:815, 1920.

The conditions under which the children of the various parts of Germany and Austria are living make it very necessary for the physicians to be acquainted with the differential diagnostic points of the parasitic diseases of the hair and scalp. Differentiation is based on three points: (*a*) the clinical picture and course of the disease; (*b*) the microscopic findings of hair examinations, and (*c*) the appearance of cultures.

The efficacy of a concentrated solution of hydrogen peroxid is mentioned, not only for the superficial trichophytosis but for pityriasis versicolor.

TENTATIVI DI RIPRODUZIONI SPERIMENTALE DEL RINOSCLEROMA NELLA SCIMMIA (AN EXPERIMENTAL ATTEMPT TO PRODUCE RHINOSCLEROMA IN APES). A. Pasini, Gior. ital. d. mal. ven. **61**:336 (Aug. 12) 1920.

Two specimens, male and female, of Papio Sphinx were used for these experiments. A fresh culture of Frisch's bacillus was injected in the upper lip, in the nasal sulcus and in the mucosa of the nose of both animals. The results were disappointing. The author reviews the reports of previous attempts of the same nature.

Pardo-Castello, Havana.

UEBER DEN THERAPEUTISCHEN EINFLUSS DER ULTRAVIOLETTEN STRAHLEN AUF DIE DERMATITIS HERPETIFORMIS (THE THERAPEUTIC EFFECT OF THE ULTRAVIOLET RAY ON DERMATITIS HERPETIFORMIS). S. Ehrmann, Arch. f. Dermat. u. Syph. **123**:517, 1916.

Professor Ehrmann, on whose service Lier did his work with the roentgen-ray on Duhring's disease, reports very good results with the use of the ultraviolet ray for the same condition. Indeed, he maintains that the good effects are more lasting as there was no relapse in a patient who did suffer a relapse following roentgen-ray treatment. This patient was free of symptoms for ten months.

GOODMAN, New York.

CURIETHERAPIE DES RADIODERMITES EPITHELIOMATEUSES PROFESSIONNELLES (RADIUM TREATMENT OF RADIODERMATITIS). DEGRAIS and BELLET, Presse méd. **28**:364 (June) 1920.

The authors emphasize the excellent results which can be obtained in chronic radiodermatitis by radium treatments without the sacrifice of the affected members which is usually advised by the surgeon. They report three cases of professional radiodermatitis which showed keratoses, indolent ulcerations and epitheliomatous formations on the hands. Healing took place under radium treatment and the intense pain also responded to this form of therapy.

KETRON, Baltimore.

SOME VIEWS ON THE TREATMENT OF SYPHILIS CONGENITA. GÖSTA AHMAN, Acta Dermato-Venereologica **1**:109, 1920.

The author agrees with Almkvist in recommending the continuous treatment. The mother should be treated energetically during pregnancy, and the infant should be kept at the breast while its treatment is intensively continued. Salicylate is the preferred mercurial, given intramuscularly. The new salvarsan-sulphaxylate is but slowly oxidizable, and Ahman has found it valuable for intramuscular injection.

PARKHURST, New York.

ZUR PROTEINKOERPERTHERAPIE UNTER BESONDERER BERUECKSICHTIGUN DER SYPHILIS (PROTEIN THERAPY WITH SPECIAL REFERENCE TO SYPHILIS). KARL SCHREINER, Wien. klin. Wchnschr. **33**:748, 1920.

Cases of sycosis vulgaris, lupus vulgaris, scrofuloderma and uncomplicated posterior urethritis (gonorrheal) have been successfully treated with injections of milk, according to the method of Schmidt. Theoretically, there appeared to be indications for the use of milk in syphilis. About twenty patients received injections, but only about half remained under observation. Only one of the ten showed recidive lesions. This case was exceptional in that it did not clear up while the patient was receiving injections. Schreiner reports that lesions of the skin and mucous membranes are favorably affected and that clinically the symptoms disappear after three injections of milk, one given every other day. With arsphenamin he asserts, at least fifteen days elapse before an equivalent result is obtained.

The injections of milk, combined with injections of small doses of neoarsphenamin, have given most excellent results; Wassermann reactions, positive before an injection, have been negative the same afternoon following the injection. The author wishes to collect the data of a larger number of cases observed over a longer period of time before giving definite conclusions.

Similar results without the by-effects of milk have been attained by the intravenous injection of peptone.

GOODMAN, New York.

A FEW CLINICAL OBSERVATIONS ON THE USE OF RADIUM IN MALIGNANT DISEASE. Thomas H. Kellock, Arch. Radiol. & Electroth. **25**:46 (July) 1920.

The writer, after citing cases of rapid early metastases in distant and unconnected parts of the body (abdomen and groins secondary to tongue, rectum secondary to jaw, and other parts) after the local use of radium, infers that such conditions must be embolic or carried by the blood. He advocates the use of radium in a different area, ten or fourteen days before treating the lesion itself, to stimulate a degree of general immunity as a prophylactic measure against metastases. Some other observations by the writer are that the best permanent results seem to follow the use of radium about the periphery of a large growth rather than its insertion into the mass; that radium has more effect in real metastasis than on local recurrences or secondarily infected lymphatic glands; that the action of radium on malignant growths is more marked in cases that are free from septic infection, and that the first application of radium has more effect than any subsequent application.

H. R. Foerster, Milwaukee.

TREATMENT OF RINGWORM. W. P. Elford, Brit. M. J. **1**:867 (June 26) 1920.

The author reports the cure of sixty cases of tinea tonsurans. The majority of patients were cured within a month's time. He used this method:

The affected area of the scalp is shaved and cleansed with liquid ethereal soap. The part is then gently and carefully rubbed with a piece of lint that has been dipped in potassium hydroxid solution and dried with a piece of absorbent cotton. The part is then sprayed with ethyl chlorid for about thirty seconds, and allowed to dry. It is then painted with diluted tincture of iodin. With the exception of shaving, the remainder of the procedure should be carried out morning and evening for the first three days, and once daily during the subsequent four or five days.

During this time a mild folliculitis occurs, and as a result the infected hairs fall out. Usually a week of such treatment is sufficient to effect a cure, after which it is only necessary to rub ammoniated mercury ointment into the scalp twice daily, keeping the case under observation for two or three weeks.

Oliver, Chicago.

TREATMENT OF VASCULAR NEVI WITH RADIUM. D. W. Montgomery and G. D. Culver, Boston M. & S. J. **183**:412 (Sept. 30) 1920.

In this article are reported four cases of vascular nevi of the face and arm. The results obtained are described as extremely good. Treatments were given every three months. The authors caution against treating before complete shrinkage has taken place. A plaque the size of a ten-cent piece, containing 25 mg. of radium, is used. This is screened with 1 mm. of lead, 2 mm. of wood, 12 thicknesses of gauze, and 1 thickness of zinc oxid adhesive plaster to hold them together. The applicator is retained in place for five hours and no burning results from this dose, although sufficient radiation goes through this material to act efficiently on the hyperplastic blood vessels of the tumor. The surrounding tissues must be well shielded with lead, leaving a hole slightly larger than the lesion. In an earlier case radium was screened with the metal capsules, which had become radioactive from contact with the radium tubes, and a burn had resulted. Under the present technic no burns have resulted, and experience shows that where the skin is not burned by the radium there are no telangiectases.

The flat, red nevus is not nearly so amenable to treatment with radium, but may be much improved. The spider nevus is not amenable to radium treatment.

UEBER DIE WIRKSAMKEIT DES ZUNTZSCHEN HAARWUCHSMITTELS "HUMAGSOLAN" (THE EFFICACY OF ZUNTZ' HAIR FOOD "HUMAGSOLAN"). HERBERT FUHS. Wien. klin. Wchnschr. **33**: 707, 1920.

Fattinger and Company of Berlin have made up a preparation of hydrolyzed horn under the name "Humagsolan." Fuhs has used the preparation in a case of alopecia areata, alopecia symptomatica (following influenza, arsphenamin dermatitis and secondary syphilis), alopecia seborrhoicum (8), and two cases with normal hair growth for control. Fuhs measured the hairgrowth, and the density of hair for weekly and biweekly periods. He is willing to conclude that the preparation is harmless for human beings, but feels that his observations were not numerous or extended enough to indicate its full therapeutic value. Observations on the growth of nails in seventeen patients were not conclusive. There is a normal variation, apparently, in nail growth (about 1.1 to 1.7 mm. for two weeks).

GOODMAN, New York.

UEBER LEUCODERMA NACH DEM SEEBADEN (LEUKODERMA FOLLOWING SEA BATHING). R. TOTSUKA, Japan. Ztschr. f. Dermat. u. Urol. **20**:5 (May) 1920.

The writer is of the opinion that the patches of leukoderma which appear after sea bathing depend on the combined action of sea bathing and sunlight. The lesions are found on the prominent parts of the trunk and on the extensor surfaces of the extremities in the form of a few, discrete, rice seed sized macules. Besides the depigmentation, the affected areas show no abnormality and there is no zone of hyperpigmentation on the periphery of the lesions. The condition appeared two weeks after the baths and in some cases disappeared spontaneously about one year after the onset.

LEVIN, New York.

QUECKSILBERINTOXIKATION NACH INJEKTIONEN VON MERZINOL (MERCURIAL POISONING AFTER INJECTIONS OF MERZINOL). MARIE KAUFMANN-WOLF, Arch. f. Dermat. u. Syph. **123**:433, 1916.

The reports of fatalities following mercury given medically are reviewed, and a case reported of a young woman who succumbed after injections of merzinol given for the treatment of latent syphilis. Although idiosyncrasy may play a part in some of the deaths reported, it is significant that women are more susceptible to this accident than men. Old age, weak constitution, underweight, anemia, nephritis, tuberculosis, myocarditis, alcoholism, poor condition of the gums and chronic angina should be considered as relative contraindications.

Gray oil has been found to be the most dangerous preparation, because the symptoms of its bad effects are not immediately apparent, and the injections are continued until the severe toxic results are introduced.

Goodman, New York.

ANTIMONY IN LEPROSY. P. G. Cawston, Brit. M. J. **2**:76 (July 17) 1920.

The author reports four cases of leprosy treated with injections of antimony. He used Oppenheimer's colloidal antimony, in doses ranging from 1 to 4 c.c. The injections were administered intramuscularly and were given daily. He concluded that intramuscular injections had a decided effect on the changes produced in a patient when *B. leprae* is at all active. It seemed to have a beneficial effect on the general condition of leper patients.

Oliver, Chicago.

UEBER DIE THERAPIE DER DERMATITIS HERPETIFORMIS DUHRING DURCH ROENTGENSTRAHLEN (THE TREATMENT OF DERMATITIS HERPETIFORMIS WITH ROENTGEN RAY). Wilhelm Lier, Arch. f. Dermat. u. Syph. **123**:506, 1916.

Three patients who were under observation for a period of several years were resistant to every conventional form of treatment for Duhring's disease. The roentgen ray (dosage, 3 H.) gave immediate relief. At the time of publication of the article, a review of the literature gave but one instance of the roentgen-ray treatment of this affection.

THE PREDOMINANCE OF SEBORRHEIC ECZEMA IN EARLY LIFE. Thomas S. Southworth, Arch. Pediat. **37**:338 (June) 1920.

In the author's experience, the predominating cases of eczema in ordinary pediatric practice are associated with seborrhea. In all such cases he recommends a careful examination of the scalp and the regions about and behind the ears. This type of eczema seemingly has a predilection for fat babies fed on breast milk rich in fat and for bottle babies suffering from disordered digestion caused by a relatively excessive intake of fat.

He believes that a seborrheic tendency forms a suitable medium for the development of dermatitis and mixed infections.

Oliver, Chicago.

LEUKOPLAKIA OF THE BLADDER AND URETER. Herman L. Kretschmer, Surg., Gynec. & Obst. **31**:325, 1920.

Kretschmer adds the report of a case to the forty-three already recorded of leukoplakia of the bladder and ureter. Only the opportunity to perform a necropsy on his patient led to the definite finding of leukoplakia of the ureter in addition to the finding of leukoplakia of the bladder. The patient was not syphilitic.

Goodman, New York.

THE TREATMENT OF MALIGNANT DISEASE BY ALTERATIVE AND CONSTRUCTIVE MEASURES. William Benham Snow, Am. J. Electroth. & Radiol. **38**: (Sept.) 1920.

The writer advocates graded small dosage with continuous tissue saturation as against the single "knock-out" blow in roentgen ray and radium treatment. He proposes radium for superficial growths, roentgen-ray treatment for deep seated tumors, and the conjoint use of the high frequency current to induce hyperemia in the tumor masses and of desiccation or electrolysis to remove the diseased tissue. In some cases he prefers that the latter methods alone be employed. Thorough roentgen-ray treatment both before and after operation is urged in the management of malignant conditions, such as breast and pelvic diseases.

H. R. Foerster, Milwaukee.

UEBER EINEN FALL VON NAEVUS UNILATERALIS COMEDO FOLLICULARIS (REPORT OF A CASE OF NEVUS UNILATERALIS COMEDO FOLLICULARIS). Menahem Hodara, Arch. f. Dermat. u. Syph. **123**:409, 1916.

Clinically the case presented large comedones in lines and groups, and brown, small, flat papules and striae. Histologically, in addition to the changes seen in nevus linearis verrucosis, one saw vascular and inflammatory changes of the cutis; acanthosis and hyperkeratosis of the epidermis, and as a special change, the formation of innumerable pseudocomedones. About several of these comedones one found a proliferation of the prickle cell layer and new formation of follicular cylindrical cells which form themselves into small follicles, from the center of which in some cases rises a newly formed hair with complete bulb root.

Goodman, New York.

MALIGNANCY OF THE CROWN-GALL AND ITS ANALOGY TO ANIMAL CANCER. Isaac Levin and Michael Levine, J. Cancer Res. **5**:243 (July) 1920.

Crown-gall occurs as a benign condition caused by *Bacterium tumefaciens* and is analogous to granuloma or keloid in man, and as a malignant condition not directly caused by the aforesaid bacterium and analogous to animal cancer.

H. R. Foerster, Milwaukee.

DIE BESEITIGUNG DES FRAUENBARTES (THE REMOVAL OF THE BEARD OF WOMEN). Max Joseph, Arch. f. Dermat. u. Syph. **123**: 425, 1916.

Joseph gives the following principles for the handling of this type of case:

Electrolysis is to be employed in cases in which the hairs are not too numerous and are thick and bristle-like.

Peroxid of hydrogen or radium is recommended for soft fine hairs.

Roentgen ray or pumice stone are the only two to be considered in full fledged hypertrichosis cases.

Goodman, New York.

EIN SELTENER FALL VON ANTIPYRINEXANTHEM (AN UNUSUAL CASE OF ANTIPYRENE EXANTHEMA). Harold Boas, Dermat. Wchnschr. **71**:479 (July) 1920.

The author reports a case of an antipyrene rash in a young girl, consisting of localized areas of edema chiefly on the genitalia.

Ketron, Baltimore.

ZUR KENNTNIS DES WANZENGIFTES (CONTRIBUTION TO THE STUDY OF BEDBUG POISON). E. Klausner, Arch. f. Dermat. u. Syph. **123**:443, 1916.

The secretion of over 50,000 bedbugs was extracted in alcohol, and used in the experiments of Klausner, who says that the active principle of the bedbug secretion is soluble in water and alcohol; that it has an intensive urticarial and hemolytic effect; that free formic acid is not present in the secretion and does not come under consideration as the cause of its effects; and that an immunization against the poisonous effects of the secretion does not seem attainable.

STUDIEN UEBER NUKLEINWIRKUNG (STUDIES ON THE ACTION OF NUCLEIN). Paul Habetin, Wien. klin. Wchnschr. **33**:726, 1920.

Habetin has studied the action of sodium nucleinate substituted for ordinary antigens in the Wassermann reaction. Fifty-eight cases were investigated. In thirty-seven there was agreement in inhibition; in eleven cases the Wassermann reaction was positive, and the sodium nucleinate antigen negative; in four cases the reverse occurred; and in six instances both tests were negative. In this series all serums were from known positive syphilitic patients.

Among thirty-eight control examinations, three patients gave positive nuclein tests. Two of these patients had malaria; the third may have been a latent syphilitic with no knowledge of his infection, who temporarily gave a negative Wassermann reaction.

Goodman, New York.

A REPORT OF THE WORK CARRIED OUT AT THE RADIUM INSTITUTE DURING 1919. A. E. Hayward Pinch, Arch. Radiol. & Electroth. **240**:50 (July) 1920.

This is a report dealing with radium salts and emanation, screening, technic, dosage and exposure, reactions, sequelae and the effects of radium radiation on radium workers, and protective measures for the latter.

H. R. Foerster, Milwaukee.

WEITERER BEITRAG ZUR FRAGE DER GOLDSOLREAKTION IM LIQUOR SEKUNDAERSYPHILITSCHER (ADDITIONAL DATA ON THE COLLOIDAL GOLD REACTION OF THE CEREBROSPINAL FLUID IN SECONDARY SYPHILIS). J. Kyrle, R. Brandt and F. Mras, Wien. klin. Wchnschr. **33**:745, 1920.

A persistent positive colloidal gold test, even in association with other negative findings is not a favorable prognostic symptom. Rarely has a case been encountered in which the colloidal gold test has been persistently negative and the Wassermann test positive, as the only symptom.

As mentioned in their earlier paper (abstracted in the October issue, p. 513), it is difficult to render the colloidal gold reaction negative even with most intensive treatment, except in those cases in which the change in this reaction is recognized to be only a slight one.

Goodman, New York.

TUBERCULOSIS VERRUCOSA CUTIS OF THE FOOT. T. McCRIRICK, Brit. J. Child. Dis. Nos. 193-195:26 (Jan.-March) 1920.

The lesion occurred on the sole of a 12 year old boy. There was active tuberculosis in the family, and it is assumed that the boy, who went barefoot, was inoculated with tuberculosis sputum in a bruise or cut.

H. R. FOERSTER, Milwaukee.

THE OCCURRENCE OF URTICARIA AFTER SPECIFIC FEVERS. E. WARD, Brit. M. J. **2**:278 (Aug. 21) 1920.

The author reports a number of cases of urticaria developing after specific fevers, pneumonia, influenza and other conditions.

OLIVER, Chicago.

UNUSUAL BENIGN EPITHELIAL TUMOR OF THE LID. S. R. GIFFORD, Am. J. Ophth. **3**:602 (Aug.) 1920.

This is a report of a case of a small fibrous nodule, without apparent connection with the overlying epidermis, showing encapsulated nests of epithelial cells with pearl formation and hyaline degeneration.

H. R. FOERSTER, Milwaukee.

TUBERCULOSIS CUTIS VEGETANS. CHRISTIAN VOGEL, Dermat. Wchnschr. **71**:560 (Aug.) 1920.

This is a case report.

KETRON, Baltimore.

BASAL CELL EPITHELIOMA OF THE CONJUNCTIVA. DAVID H. COOVER, Am. J. Ophth. **3**:683 (Sept.) 1920.

The author reports the case of a fungoid tumor microscopically diagnosed as prickle cell epithelioma occurring on the site of a papilloma removed eleven years previously. The eyeball was removed.

H. R. FOERSTER, Milwaukee.

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